Title

An evaluation of the effectiveness and cost-effectiveness of screening for diabetic retinopathy by digital imaging photography and technician ophthalmoscopy and the subsequent change in activity, workload and costs of new diabetic ophthalmology referrals.

Submission for the degree of MD

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Abstract

Aims:

1) To validate an Ophthalmologists reference standard examination.
2) To evaluate the effectiveness and cost-effectiveness of the introduction of a community based non-mydriatic and mydriatic digital photographic screening programme for diabetic retinopathy.
3) To determine the subsequent change in workload of the Ophthalmology Department.

Methods:

1) An Ophthalmologist's examination was compared prospectively with 7-field stereo-photography in 239 persons.
2) 3611 patients attending general practices in Gloucestershire had one-field, non-mydriatic and mydriatic two-field digital photography. 1549 of these patients were examined by an Ophthalmologist. A cost effectiveness analysis was undertaken.
3) A retrospective study of Eye clinic workload was performed for the year before screening commenced, 2 years of the first round and the first year of the second round.

Results:

1) In comparison with 7-field stereo photography, the Ophthalmologist's examination gave a sensitivity of 87.4% (confidence interval 83.5–91.5%) and a specificity of 94.9% (91.5-98.3%).
2) For mydriatic digital photography, the sensitivity was 87.8%, specificity was 86.1% and technical failure rate was 3.7%. For non-mydriatic photography, the sensitivity was 86.0%, specificity was 76.7% and technical failure rate was 19.7%. The best estimate of cost per true positive detected was £429 (range £394-£473) for mydriatic and £490 (£450-£535) for non-mydriatic photography.
3) The annual referral rate and the number with diabetes in the county increased over the four years and only reduced in the fourth year for laser treatment sessions (171, 282, 265, 199).

Conclusions:

Two-field mydriatic digital photography is an effective and cost-effective method of screening for referable diabetic retinopathy whereas non-mydriatic digital photography has an unacceptable technical failure rate and low specificity. The consequent

workload in the Eye clinic increased in the first round of screening but, with increasing numbers of people with diabetes, did not fall below the pre-screening level, except for laser treatment.

KEY WORDS
Diabetic Retinopathy
Ophthalmoscopy
Screening
Digital Photography
Sensitivity and Specificity

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Table of Abbreviations

ABCD	Appropriate Blood Pressure Control in Diabetes Trial
AION	Anterior Ischaemic Optic Neuropathy
ARMD	Age Related Macular Degeneration
AusDiab	Australian Diabetes, Obesity and Lifestyle Study
BCVA	Best Corrected Visual Acuity
BDA	British Diabetic Association (now Diabetes UK)
BD8 forms	Blindness registration forms
BDR	Background diabetic retinopathy
BMJ	British Medical Journal
BRVO	Branch retinal vein occlusion
CCD camera	Charge coupled device
CI	Confidence interval
CLBM	Contact lens biomicroscopy
CRAO	Central Retinal Artery Occlusion
CRVO	Central Retinal Vein Occlusion
CSMO (CSME)	Clinically significant macular oedema (in American studies referred to as CSME)
CWS	Cotton wool spot
DCCT	Diabetes Control and Complications Trial

DH	Department of Health
DR	Diabetic retinopathy
DRSRG	Diabetic Retinopathy Study Research Group
DD	Disc diameter
ETDRS	Early Treatment Diabetic Retinopathy Study
EURODIAB	EURODIAB Insulin Dependent Diabetes Mellitus Complications Study
FDR	Florid diabetic retinopathy
GDESS	Gloucestershire Diabetic Eye Screening Service
HE	Hard exudate
HL	Helen Lipinski (Senior Grader at the Retinopathy Grading Centre)
HTBS	Health Technology Board for Scotland
IDDM	Insulin Dependent Diabetes Mellitus
IRMA	Intra retinal microvascular anomaly
JISC	Joint Information Systems Committee
JPEG	Joint Photographic Experts Group compression
LogMAR	Logarithm of the minimum angle of resolution
MA	Microaneurysm
MIMAS	Manchester Information and Associated Services
MDI	Medical Data Index
MRI	Magnetic Resonance Imaging
NOP	Non-ophthalmic practitioner
NSC	National Screening Committee
NVD	Neovascularisation of the disc
NVE	Neovascularisation elsewhere
NFL	Nerve fibre layer
NICE	National Institute for Clinical Excellence
NIDDM	Non-insulin-dependent diabetes mellitus
NPDR	Non-proliferative diabetic retinopathy
NSF	National Service Framework
OFA	Oral fluorescein angiography
OMP	Ophthalmic Medical Practitioner
PAS	Patient administration system

PPDR	Pre-proliferative diabetic retinopathy
PPV	Pars plana vitrectomy
PCIOL	Posterior chamber intraocular lens
PDR	Proliferative diabetic retinopathy
-PRP	Pan retinal photocoagulation
QALY	Quality-adjusted life-year
RM	Raman Malhotra (Specialist Registrar in Ophthalmology)
RPE	Retinal pigment epithelium
RTA	Retinal thickness analyser
SIGN	Scottish Intercollegiate Guidelines Network
SPR	Specialist Registrar
STED	Sight threatening eye disease
STDR	Sight threatening diabetic retinopathy
TFT	Thin film transistor
TIFF	Tagged Image File Format
TCT	Tritan contrast threshold
UKPDS	United Kingdom Prospective Diabetes Study
VB	Venous beading
VA	Visual acuity
VISS	Vascular complications in South-east Sweden Study
WESDR	Wisconsin Epidemiological Study of Diabetic Retinopathy
WHO	World Health Organisation

1 Introduction.

The definition of screening that was adapted by the WHO[1] in 1968 was 'the presumptive identification of unrecognised disease or defect by the application of tests, examinations or other procedures which can be applied rapidly. Screening tests sort out apparently well persons who probably have a disease from those who probably do not. A screening test is not intended to be diagnostic. Persons with positive or suspicious findings must be referred to their physicians for diagnosis and necessary treatment.'
The principles for screening for human disease that were derived from the public health papers produced by the WHO[1] in 1968 were:

1. The condition sought should be an important problem.
2. There should be an accepted treatment for patients with recognised disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognisable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of the case-finding programme (including early diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a 'one-time' project.

Applying these principles to sight-threatening diabetic retinopathy raises the following questions:

1. Is there evidence that sight-threatening diabetic retinopathy is an important public health problem?
2. Is there evidence that the incidence of sight-threatening diabetic retinopathy is going to remain the same or become an even greater public health problem?
3. Is there evidence that sight-threatening diabetic retinopathy has a recognisable latent or early symptomatic stage?

4. Is there evidence that treatment for sight-threatening diabetic retinopathy is effective and agreed universally?
5. Is a suitable and reliable screening test available, acceptable to both health care professionals and (more importantly) to the public?
6. Are the costs of screening and effective treatment of sight-threatening diabetic retinopathy balanced economically in relation to total expenditure on health care - including the consequences of leaving the disease untreated?

1.1 Methodology of the literature review.

Study selection - articles were selected to help answer the questions posed in the introductory section.

Relevant articles were identified from the following sources:

1. Prominent review articles and reports such as those by:
   a) MacCuish AC[2], in 1992.
   b) Singer DE[3], in1992.
   c) The Scottish Health Purchasing Information Centre[4] report entitled 'Preventing blindness in Diabetes' in1996.
   d) Bachmann and Nelson[5], in 1996.
   e) The Royal College of Ophthalmologists report entitled 'Guidelines for Diabetic Retinopathy' in 1997.
   f) Hutchinson A[6], in 2000.
   g) Report for the UK National Screening Committee[7-9] in 2000.
   h) National Institute for Clinical Excellence[10] final draft report entitled 'Screening and early management of diabetic retinopathy in Type 2 diabetes' in 2000.
   i) The Scottish Intercollegiate Guidelines Network[11] (SIGN) in 2001.
   j) The Health Technology Board for Scotland[12] entitled 'Organisation of Services for Diabetic Retinopathy Screening' in 2002.
   k) National Institute for Clinical Excellence Guideline[13] for Type 2 diabetes entitled 'Retinopathy - screening and early management' in 2002.
   l) National Service Framework for Diabetes[14]: Delivery Strategy in 2002.
   m) Health Technology Assessment Report[15] by Sharp et al entitled 'The value of digital imaging in diabetic retinopathy' in 2003.
   n) National Institute for Clinical Excellence[16] draft report entitled 'Type 1 diabetes: management of Type 1 diabetes in adults in primary and secondary care'.
2. Recommendations from colleagues.
3. A MEDLINE search (January 1986 to April 2000).
4. Additional references were selected from the bibliographies of identified articles.
5. Since March 2000, a search technique was used with Zetoc, which is a co-operative venture between the British Library, Manchester Information and Associated Services (MIMAS) and the Joint Information Systems Committee (JISC) of the UK Higher Education Funding Council (http.//zetoc.mimas.ac.uk). It is available to English NHS regions and NHS Scotland. Zetoc provides access to the British

Library's Electronic Table of Contents of around 20,000 of the most important research journals worldwide and around 16,000 conference proceedings published per year. The database covers 1993 to date and is updated on a daily basis. It enables the researcher to search for articles as well as conference papers with a direct link to the British Library to order them.

The following subject title keywords were set up:

Blindness
Diabetic retinopathy
Digital imaging
Laser
Retinopathy
Screening
Visual acuity
Visual impairment.

The journals selected for contents page lists were:

Acta Ophthalmologica Scandinavia
American Journal of Ophthalmology
Archives of Ophthalmology
British Journal of Ophthalmology
British Medical Journal
Clinical and Experimental Ophthalmology
Diabetes
Diabetes Care
Diabetes Metabolism Research and Reviews
Diabetes Research and Clinical Practice
Diabetes Technology and Therapeutics
Diabetic Medicine
Diabetologia
European Journal of Ophthalmology
Eye
Graefes Archive for Clinical and Experimental Ophthalmology
Japanese Journal of Ophthalmology.

Whole articles required from the contents page or from the keyword searches were requested directly from the local NHS Trust library or on-line from the Athens resource available to the Trust library.

1.2.1 Is there evidence that sight-threatening diabetic retinopathy is an important public health problem?

1.2.1.1 Studies reporting the prevalence of diabetic retinopathy.

Three studies have given strong evidence that sight-threatening diabetic retinopathy is prevalent and numerous other studies have supported this viewpoint. These three studies are by Klein[17 18], Kohner[19] and Younis[20].

In 1992, Klein[17] reported results from the Wisconsin Epidemiological Study of Diabetic Retinopathy (WESDR study), which was a population-based study in southern Wisconsin of 996 insulin-taking younger-onset diabetic persons (given diagnoses of diabetes under 30 yrs) and 1,370 patients given diagnoses of diabetes at age 30 years or older who were examined using standard protocols to determine the prevalence and severity of diabetic retinopathy and associated risk variables. Proliferative Diabetic Retinopathy (PDR) was found to be a prevalent complication - 23% in the younger-onset group, 10% in the older-onset group that takes insulin, and 3% in the group that does not take insulin. In 1995 Klein[18] reported the incidence of macular oedema over a 10-year period. This was 20.1% in the younger-onset group, 25.4% in the older-onset group taking insulin, and 13.9% in the older-onset group not taking insulin.

In 1998, Kohner[19] reported baseline retinopathy levels in 2964 patients with diabetes enrolled in the United Kingdom Prospective Diabetes Study (UKPDS). Retinopathy, defined as microaneurysms or worse lesions in at least 1 eye, was present in 39% of men and 35% of women. Marked retinopathy with cotton wool spots or intraretinal microvascular abnormalities was present in 8% of men and 4% of women.

In 2002, Younis[20] reported baseline results from population screening in Liverpool of 831 people with Type 1 diabetes and 7231 people with Type 2 diabetes. The results showed a baseline for Type 1 of any DR 45.7%, PDR 3.7% and STED 16.4%. Baseline for Type 2 group of any DR 25.3%, PDR 0.5% and STED 6.0%.

Kernell[21]reported the youngest child in the literature (11.8 years) with pre-proliferative DR. Donaghue[22] reported the youngest child reported in the literature with background diabetic retinopathy - 7.9 yrs (duration 5.6 years, HbA1c 8.9%). Bailey[23] reported high levels of visual symptomatology in patients with sight-threatening diabetic retinopathy. Other studies that have reported on the prevalence of diabetic eye disease have been by Scobie[24], Foulds[25], McLeod[26], Sparrow[27], Joner[28], McKay[29], Ramachandran[30], Rema[31], Hesse[32], Malone[33], West[34], Klein[35], Kullberg[36], Liu[37] and Tapp[38].

There has been a recently published systematic review by Williams[39] on the epidemiology of diabetic retinopathy and macular oedema. This article concludes that studies of sufficient size to stratify for age and duration of eye disease show an increase in DR in older age groups with long-standing disease.

1.2.1.2 Reports on blindness and visual impairment.

The majority of studies recorded above report that sight-threatening diabetic retinopathy and consequent visual impairment are prevalent and are therefore an important public health problem.

In 1980, Ziemianski[40] reported on 85 eyes with severe vitreous haemorrhage on initial visit. Ultimately 68% of the eyes (over a 10 yr follow-up) had a visual acuity of 5/200 or worse. In 1990, the St Vincent Declaration[41] recognised diabetes and diabetic retinopathy to be a major and growing European health problem, a problem at all ages and in all countries. The first of the five-year targets that were unanimously agreed by Government Health Departments and patient's organisations from all European countries was to reduce new blindness due to diabetes by one third or more. In 1994, Moss[42] reported on the 10-year incidence of blindness in the WESDR study. 1.8%, 4.0%, and 4.8% in the younger-onset, older-onset taking insulin, and older-onset not taking insulin groups, respectively. Respective 10-year rates of visual impairment were 9.4%, 37.2%, and 23.9%. In 1995, Evans[43] reported on the causes of blindness and partial sight in England and Wales from an analysis of all BD8 forms for the year April 1990 to March 1991. Among people of working age (ages 16-64), diabetes was the most important cause (13.8%) with 11.9% due to diabetic retinopathy.

Other reports of blindness due to diabetic eye disease have been by Clark[44], Fong[45], Roy[46], Cormack[47], Prasad[48], Miki[49] and Hayward[50].

In 2001, Cunningham[51] reported that 45 million people worldwide fulfill the World Health Organisation's criterion for blindness and the cause of one quarter of all blindness, which affects people in both developed and developing nations, includes diabetic retinopathy and macular degeneration. In 2002, Kocur[52] reported that in people of working age in Europe, diabetic retinopathy is the most frequently reported causes of serious visual loss.

1.2.2 Is there evidence that the incidence of sight-threatening diabetic retinopathy is going to remain the same or become an even greater public health problem?

Numerous studies have shown that there is a rising incidence of diabetes and it's complications in all age groups, both in the UK and worldwide. In 1997, Amos[53] estimated that 124 million people worldwide have diabetes, 97% NIDDM and that by 2010 the total number with diabetes is projected to reach 221 million. In 2000, Sorensen[54] reported that the World Health Organisation has recognised that there is a "global epidemic of obesity" and the prevalence of type 2 diabetes is rising in parallel. In 2001, Boyle[55] estimated the number of Americans with diagnosed diabetes is projected to increase from prevalence of 4.0% in 2000 to a prevalence of 7.2% in 2050. Other reports describing the rising incidence of diabetes are from Burrows[56], Ehtisham[57], Sidibe[58], Mokdad[59 60] and Feltbower[61].

1.2.3 Is there evidence that sight-threatening diabetic retinopathy has a recognisable latent or early symptomatic stage?

In 1981, Palmberg[62] described a study of the natural history of diabetic retinopathy in 461 people with juvenile-onset IDDM. At diagnosis no DR was found, at 7 yrs 50%, at 17-50 yrs 90%. Proliferative Diabetic Retinopathy (PDR) was first seen at 13 yrs, 26% at 26-50 yrs.

In 1984 and 1989, Klein[63 64 65 66]reported on the natural history of Diabetic Retinopathy in the Wisconsin Epidemiological Study (WESDR study). For the 996 insulin-taking younger-onset people with diabetes (given diagnoses of diabetes under 30 yrs), the prevalence of any DR was 17% < 5 yrs, 97.5% ≥ 15yrs. The prevalence of PDR was 1.2% < 10 yrs, 67% ≥ 35yrs. For the 271 people with IDDM diagnosed < 30 yrs with no DR at first visit in WESDR, 59% developed DR after 4 yrs. For the 713 people with IDDM diagnosed < 30 yrs with no PDR at first visit, 11% developed PDR after 4 years. Worsening of DR occurred in 41%, improvement in 7%. Incidence of PDR rose to 14% after 13yrs of diabetes. For the 1,370 patients given diagnoses of diabetes at age 30 years or older the prevalence of any DR was 28.8% < 5 yrs, 77.8% ≥ 15yrs. The prevalence of PDR was 2.0% < 5 yrs, 15.5% ≥ 15yrs. For the 154 people with IDDM diagnosed ≥ 30 yrs with no DR at first visit, 47% developed DR after 4 yrs. For the 418 people with IDDM diagnosed ≥ 30 yrs with no PDR at first visit, 7% developed PDR after 4 years and worsening of DR in 34%. For the 320 non IDDM diagnosed ≥ 30 yrs

with no DR at first visit, 34% (developed DR after 4 yrs. For the 486 non IDDM diagnosed ≥ 30 yrs with no PDR at first visit, 2% developed PDR after 4 years and worsening of DR in 25%.

Further studies that have shown clear evidence that sight-threatening diabetic retinopathy has a recognisable latent or early symptomatic stage have been reported by Frank[67], Klein[68], Burger[69], Kohner[70], ETDRS[71 72], Aldington[73], Klein[74], Danne[75], Klein[76], Ling[77] and Younis[78 79].

1.2.4 Is there evidence that treatment for sight-threatening diabetic retinopathy is effective and agreed universally?

1.2.4.1 The evidence that laser treatment is effective.

Since Spalter[80] described the photocoagulation of circinate maculopathy in diabetic retinopathy, clear evidence for the efficacy of laser treatment for diabetic eye disease has been shown from the Diabetic Retinopathy Study[80 81 82 83] and the Early Treatment Diabetic Retinopathy Study [84 85 86]. In 1976, the organisers of the Diabetic Retinopathy Study[80] modified the trial protocol and recommend treatment for control eyes with 'high risk characteristics'. In 1979, they reported[81] four retinopathy factors that increase the two-year risk of developing severe visual loss.

(1) The presence of vitreous or preretinal haemorrhage;

(2) The presence of new vessels;

(3) The location of new vessels on or near the optic disc;

(4) The severity of new vessels.

In 1981 they reported[82] that photocoagulation, as used in the study, reduced the two-year risk of severe visual loss by 50% or more.

In 1985, a report[84] from the Early Treatment Diabetic Retinopathy Study showed that focal photocoagulation of "clinically significant" diabetic macular oedema (CSMO) substantially reduced the risk of visual loss.

Further studies that have shown evidence for the efficacy of laser treatment for diabetic eye disease have been reported by Whitelocke[87], British multicentre study[88], Blankenship[89], Bailey[90 91] and Chew[92].

1.2.4.2 The evidence that Vitrectomy for more advanced disease is effective.

Smiddy[93] wrote an excellent review in 1999 when he noted that, according to the Early Treatment Diabetic Retinopathy Study, at least 5% of eyes receiving optimal medical treatment will still have progressive retinopathy that requires laser treatment and pars plana vitrectomy. He also noted that, although vitrectomy improves the prognosis for a favourable visual outcome, preventive measures, such as improved control of glucose levels and timely application of panretinal photocoagulation, are equally important in the management. Vitrectomy clearly does have a place in the management of diabetic eye disease. Evidence of improving visual results during the last 20 years following vitrectomy have been shown in studies reported by Blankenship[94], Thompson[95 96-98], Sigurdsson[99], Flynn[100], Nakazawa[101], Karel[102], Harbour[103], Pendergast[104], La Heij[105], Yamamoto[106], Amino[107], Lewis[108] and Lahey[109].

1.2.4.3 The evidence that diabetic retinopathy can be prevented or the rate of deterioration reduced by improved control of blood glucose, blood pressure and lipid levels and by giving up smoking.

In 1976, Cahill[110] wrote that the weight of evidence strongly supports the concept that the microvascular complications of diabetes are decreased by reduction of glucose concentrations. In 1981, Hyman[111] recommended a nationally co-ordinated clinical study of sufficient duration to resolve the issue. Evidence for the link between poor glucose control and greater progression of diabetic retinopathy was provided by Frank[67], Dahl-Jorgensen[112], Brinchmann-Hansen[113], Joner[28], Klein[17], Danne[114], Klein[18], Davis[115], Klein[76], Fong[45].

The study that changed opinion and confirmed that intensive blood glucose control reduces the risk of new onset DR and slows the progression of existing DR for patients with IDDM was the Diabetes Control and Complications Trial[116 117 118] (DCCT). The trial included 1441 people with IDDM, 726 with no DR at base line (the primary-prevention cohort), and 715 with mild retinopathy (the secondary-intervention cohort), with mean follow-up of 6.5 years. For the primary-prevention cohort, intensive therapy reduced the mean risk for the development of DR by 76 % (CI 62-85 %), compared with conventional therapy. For the secondary-intervention cohort, intensive therapy slowed the progression of DR by 54 % (CI 39-66 %) and reduced the development of PDR or severe NPDR by 47 % (CI 14-67 %).

The study that changed opinion and confirmed that intensive blood glucose control reduces the risk of new onset DR and slows the progression of existing DR for patients with NIDDM was the United Kingdom Prospective Diabetes Study [19 119 120 121 122]. This study recruited 3867 with NIDDM and the effect of intensive blood-glucose control with sulphonylureas or insulin was compared with conventional treatment. Compared with the conventional group, there was a 25% risk reduction (7-40, p=0.0099) in the intensive group in microvascular endpoints, including the need for retinal photocoagulation. Patients allocated metformin, compared with the conventional group, had risk reductions of 32% (95% CI 13-47, p=0.002) for any diabetes-related endpoint.

Evidence that control of systemic hypertension reduces the risk of new onset DR and slows the progression of existing DR comes from studies reported by Chase[123], Joner[28], Klein[76], UKPDS[121], Stratton[122] and Estacio[124].

Evidence that elevated serum lipids are associated with macular exudates and moderate visual loss and partial regression of hard exudates may be possible by reducing elevated lipid levels comes from studies reported by Chew[125], Fong[45], Klein[35], Sen[126] and Cusick[127].

Smoking – there is some evidence that smoking may be a risk factor in progression of diabetic retinopathy in Type 1 diabetes as described by Muhlhauser[128 129] and Karamanos[130]. However, in Type 2 disease the evidence is controversial and it may protect[122] against the progression of retinopathy in some patients despite the fact that it is an independent risk factor for cardiovascular disease in all patients with diabetes.

1.2.4.4 The possibility of novel therapies in the future.

In 2003, Ciulla[131] reviewed novel therapies for diabetic retinopathy and diabetic macular oedema. Several biochemical mechanisms, including protein kinase C-beta activation, increased vascular endothelial growth factor production, oxidative stress, and accumulation of intracellular sorbitol and advanced glycosylation end products, may contribute to the vascular disruptions that characterise DR/DME. The inhibition of these pathways holds the promise of intervention for DR at earlier non-sight-threatening stages.

1.2.5 Is a suitable and reliable screening test available, acceptable to both health care professionals and (more importantly) to the public?

1.2.5.1 Studies of direct ophthalmoscopy.

In order to compare studies of direct ophthalmoscopy as a method of screening they have been tabulated below into similar categories and they have been further divided into those that have compared direct ophthalmoscopy with a recognised reference standard of seven-field stereo photography, an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography, and those that have not.

In those studies that compared direct ophthalmoscopy to a recognised reference standard, those by Sussman[132], Foulds[25], Kleinstein[133], Awh[134], Nathan[135] and Kinyoun[136] contained less than 100 patients.

Those studies that included more than 100 patients showed the following results: Palmberg[62] found a detection rate of any DR of 56% that of 7 field stereo in 461 patients using mydriatic direct ophthalmoscopy by Board Certified American Ophthalmologists. Moss[137] found an exact agreement 85.7% of the time between mydriatic direct ophthalmoscopy (supplemented by binocular indirect ophthalmoscopy if the examiners felt this was necessary) and grading using seven field stereo-photography for detecting level of retinopathy (none, non proliferative, proliferative) in 1949 patients. However, this was following consultation between three examiners an Ophthalmologist, a specially trained Optometrist and an ophthalmic technician. Pugh[138] found the physician's assistant sensitivity 14%, specificity 99%, Ophthalmologist sensitivity 33%, specificity 99% for the detection of retinopathy levels (dichotomised into no DR and mild NPDR versus moderate to severe NPDR and PDR) compared to seven field stereo-photography in a study of 352 patients. Harding[139] found the sensitivity achieved for the detection of sight-threatening retinopathy compared to sit-lamp biomicroscopy by a retinal specialist was only 65% (CI 51-79%).

In those studies that did not compare direct ophthalmoscopy to a recognised reference standard, very variable rates of detection were found with different professional groups compared to different reference standards. For example:

Buxton[140] compared mydriatic direct ophthalmoscopy by general practitioners (GPs), ophthalmic opticians and hospital physicians to mydriatic direct ophthalmoscopy by an ophthalmological clinical assistant in 3318 patients in three UK centres. The outcome measure was referral for sight-threatening DR. The performance of primary screeners

based on ophthalmoscopy ranged from sensitivity 41%, specificity 89%, for one of the GP groups, sensitivity 67%, specificity 96%, for the hospital physician group. Gibbins[141] reported the results of direct ophthalmoscopy by GP's, study Optometrist's and community Optometrist's compared with external grading of 2 field mydriatic 45 degree 35mm colour slide retinal images for the detection of referable DR. For direct ophthalmoscopy, GPs achieved a sensitivity of 65.7% and specificity 93.8% Community Optometrists achieved a sensitivity of 82.2% and the study Optometrist 79.2%, respectively.

In conclusion sensitivity and specificity of direct ophthalmoscopy as a method of screening show such variable results between professional groups and within professional groups that it is not to be recommended for a systematic screening programme. It is still useful for ad hoc screening and it may also be a useful adjunct to photographic screening as recommended by Ryder[142], Jacob[143], O'Hare[144],Taylor[145] and Gibbins[141].

Hence, one of the aims of the Gloucestershire Diabetic Eye study was to assess the added value of technician ophthalmoscopy to digital imaging photography using relatively inexperienced technicians (compared to those used in some previous studies[142 145]).

Studies comparing direct ophthalmoscopy with a recognised reference standard of seven-field stereo photography, an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography.

Some studies that have included binocular indirect (without slit-lamp biomicroscopy) have been included:

Year	Author	Number of patients in study (n), patients (p), eyes (e)
I981	Palmberg[62]	n = 461 p.
	Method	Mydriatic direct ophthalmoscopy.
	Professional group	Board certified Ophthalmologists.
	Reference standard	7 field stereo-photography.

	Outcome measure	Detection of DR.
	Result	Detection 56% that of 7 field stereo.
1982	Sussman[132]	n = 21 e.
	Method	Physician's mydriatic direct ophthalmoscopy and Ophthalmologist binocular indirect ophthalmoscopy. Twenty-three physicians (10 internists, 2 diabetologists, 4 senior medical residents), Ophthalmologists (4 general and 3 sub-specialists in retinal disease).
	Reference standard	7 field stereo-photography.
	Outcome measure	Detection of proliferative DR (7 of 21 eyes had proliferative DR).
	Result	The error rate for missing the diagnosis of proliferative retinopathy varied from 0% for retinal specialists, 9% for general Ophthalmologists, 33% for diabetologists, 50% for senior medical residents and 52% for internists.
1983,	Foulds[25]	n = 93 p.
	Method	Mydriatic direct ophthalmoscopy.
	Professional group	Physician or Ophthalmologist.
	Reference standard	Fluorescein angiography.
	Outcome measure	Detection of serious retinopathy.
	Sensitivity & specificity	Serious retinopathy in the random sample was 11%, detected by Physicians in 8% and by Ophthalmologist's in 7%.
1985	Moss[137]	n = 1949 p.
	Method	Mydriatic direct ophthalmoscopy, supplemented by binocular indirect ophthalmoscopy if the examiners felt this was necessary.

	Professional group	An Ophthalmologist, a specially trained Optometrist and an ophthalmic technician. Consultation among the three examiners was permitted.
	Reference standard	7 field stereo-photography.
	Outcome measure	Detection of retinopathy (none, non proliferative, proliferative).
	Sensitivity & specificity	There was exact agreement between ophthalmoscopy and grading for detecting level of retinopathy (none, non proliferative, proliferative) 85.7% of the time. The kappa statistic was 0.749.
1987	Kleinstein[133]	n = 25 e.
	Method	Mydriatic direct and/or binocular indirect ophthalmoscopes.
	Professional group	Optometrists.
	Reference standard	7 field stereo-photography.
	Outcome measure	Detection of DR of varying levels.
	Sensitivity & specificity	Sensitivity of Optometrists for diagnosis of DR using only ophthalmoscopy was 74% (95% CI: 67%, 81%), while specificity for diagnosing the absence of DR was 84% (95% CI: 73%, 96%).
1991	Awh[134]	n = 20 p.
	Method	Mydriatic direct ophthalmoscopy before and 2 weeks following the teaching session.
	Professional group	Non-Ophthalmologist physicians.
	Reference standard	7 field stereo-photography.
	Outcome measure	Detection and appropriate referral of PDR, PPDR or maculopathy.

	Sensitivity & specificity	The likelihood of failing to detect PDR or PPDR retinopathy decreased from 60% to 15%. For patients with maculopathy, the likelihood of failure to detect decreased from 83% to 15.6%.
1991	Nathan[135]	n = 67 p.
	Method	Diabetologists with non-mydriatic direct ophthalmoscopy and Ophthalmologists by mydriatic indirect binocular ophthalmoscopy (in addition slit-lamp biomicroscopy in some patients at the examiner's discretion).
	Professional group	Diabetologists with > 8 years experience in diabetes and one of two Ophthalmologists.
	Reference standard	7 field stereo-photography.
	Outcome measure	On the basis of fundus photography, patients were classified as having no or insignificant (30%), minimal (31%), moderate (24%), or severe (15%) retinopathy.
	Sensitivity & specificity	The diabetologists and Ophthalmologists performed similarly in their ability to classify severity of diabetic retinopathy accurately, with the Ophthalmologists more sensitive in detection of perimacular lesions ($p<0.05$) and macular oedema ($p<0.001$).
1992	Kinyoun[136]	59 p with Type 2 diabetes.
	Method	Mydriatic ophthalmoscopy (binocular indirect and direct) by a retina specialist.
	Professional group	Reading of 7-field photos by two groups - a trained photographic grader and a retina specialist.
	Reference standard	Seven standard field fundus photographs read by the same retina specialist.
	Outcome measure	7 levels of retinopathy P_0, P_m, P_{1-5}.

	Results	Kappa's, 0.69-0.84 between the retina specialist's and trained grader's reading of photographs, kappa's, 0.58-0.79 agreement between the retina specialist's ophthalmoscopic findings and the specialist's reading of photographs, and kappa's, 0.49-0.62 between the retina specialist's ophthalmoscopic findings and the trained grader's reading of fundus photographs. Analysis of the disagreements confirmed earlier reports that ophthalmoscopy misses approximately 50% of eyes with microaneurysms only. Other disagreements resulted from the trained grader's over-reading photographs of eyes with lesions simulating DR.
1993	Pugh[138]	n = 352.
	Method	Physician's assistant mydriatic direct ophthalmoscopy and Ophthalmologist mydriatic direct and binocular indirect ophthalmoscopy. In one of the two centres slit-lamp biomicroscopy using a 90 Dioptre lens.
	Professional group	2 physician's assistants and a total of 10 staff Ophthalmologists (2 retina specialists, 8 general Ophthalmologists and no residents) from two centres performed the ophthalmoscopy examinations.
	Reference standard	7 field stereo-photography.
	outcome measure	Retinopathy levels were dichotomised into no DR and mild NPDR versus moderate to severe NPDR and PDR.
	Sensitivity & specificity	The sensitivities, specificities, and positive and negative likelihood ratios are: physician's assistant 0.14, 0.99, 12, 0.87; Ophthalmologist 0.33, 0.99, 72, 0.67.
1995	Harding[139]	n = 326 p.
	Method	Mydriatic direct ophthalmoscopy.
	Professional group	A specialist registrar in ophthalmology.

	Reference standard	Slit-lamp biomicroscopy by a retinal specialist.
	Outcome measure	Detection of sight threatening eye disease.
	Sensitivity & specificity	Sensitivity by direct ophthalmoscopy was 65% (CI 51-79%) and specificity was 97% (CI 95-99%).

Studies of direct ophthalmoscopy without a recognised reference standard. Some studies that have included binocular indirect (without slit-lamp biomicroscopy) have been included.

1982	Gilbert[146]	n = 322 p. Reference standard examination in 31 of the 'abnormal' group and 127 of the 'normal' group.
	Method	Direct ophthalmoscopy (? non-mydriatic - not clear in this article).
	Professional group	Ophthalmic opticians.
	Reference standard	Ophthalmologist using direct and binocular indirect ophthalmoscopy after mydriasis.
	Outcome measure	Detection of any DR and retinopathy requiring laser treatment.
	Result	In the group reported as 'normal' by the opticians no patients were found to have retinopathy requiring treatment while seven were found to have background retinopathy.
1985	Burns-Cox[147]	n = 844.
	Method	Direct ophthalmoscopy (? non-mydriatic - not clear in this article).
	Professional group	Ophthalmic opticians.
	Reference standard	Ophthalmologist using direct and binocular indirect ophthalmoscopy after mydriasis.
	Outcome measure	Detection of referable retinopathy.

	Result	Out of 844 eye checks, 80 were reported by ophthalmic opticians to justify referral to an Ophthalmologist and 20 of these required photocoagulation treatment. Of a sample of 197 patients rechecked by an Ophthalmologist reported by ophthalmic opticians not to justify referral, only one needed treatment.
1987	Forrest[148]	n = 282 p.
	Method	Mydriatic direct ophthalmoscopy.
	Professional group	A specially trained nurse and a consultant diabetologist.
	Reference standard	5-field non-stereoscopic 35 mm fundal photography.
	Outcome measure	Detection of any DR. Detection of neovascularisation.
	Result	The characteristics of nurse examination as a test to detect retinopathy were: sensitivity 50.0%, specificity 99.2%, which compared with 51.3% and 98.7% for the doctor. New vessels were missed in 5 of 6 cases by the doctor.
1989	Lienert[149]	n = 500 p.
	Method	Mydriatic direct ophthalmoscopy.
	Professional group	Non-ophthalmic practitioner (NOP) - Two general practitioners examined 24 patients, 25 medical registrars examined 233 patients, 3 physicians (specialising in diabetes) examined 239 patients.
	Reference standard	Direct ophthalmoscopy by an Ophthalmologist.
	Outcome measure	Detection of levels of DR.
	Result	There was an 'under diagnosis' by the NOP's of 15 of 33 retinae showing preproliferative DR and 12 of 22 retinae showing proliferative DR.
1991	Buxton[140]	n = 3318 p in three UK centres.
	Method	Mydriatic direct ophthalmoscopy by primary screeners.

	Professional group	Primary screeners were general practitioners (GPs), ophthalmic opticians and hospital physicians.
	Reference standard	Mydriatic direct ophthalmoscopy by an ophthalmological clinical assistant.
	Outcome measure	Referral for sight-threatening DR.
	Result	The performance of primary screeners based on ophthalmoscopy ranged from sensitivity 0.41, specificity 0.89, for one of the GP groups, sensitivity 0.67, specificity 0.96, for the hospital physician group.
1991	Finlay[150]	n = 331 e (in 201 p).
	Method 1	Mydriatic direct ophthalmoscopy.
	Professional group	21 general practitioners.
	Method 2	One 45 degree field mydriatic colour-slide photograph.
	Reference standard	Mydriatic direct ophthalmoscopy by an Ophthalmologist.
	Outcome measure	Detection of any DR and sight-threatening DR.
	Result	The GP's detected retinopathy with a sensitivity of 55%, and a specificity of 85.8%. 'Sight-threatening' retinopathy was detected with 52% sensitivity and 97.4% specificity. The results for assessment of photographs were 60.2% and 96.8% for any retinopathy and 66.7% and 97% for 'sight threatening' retinopathy.
1991	Ryder[151]	
	Method 1	Direct ophthalmoscopy with mydriasis (Group 1).
	Professional group	Physicians.
	Method 2	Single 45 degree field Polaroid photography with mydriasis only if retinopathy on the Polaroid (Group 2).
	Method 3	Single 45 degree field Polaroid photography with mydriasis followed by direct ophthalmoscopy (Group 3).

	Reference standard	Nil.
	Outcome measure	Detection of any DR and good-quality photograph rates.
	Result	Clinic doctors reported DR in 9/41 (22%) Group 1 and 26/96 (27%) in Groups 2 and 3. It was only necessary to dilate about 17% of eyes to obtain >90% good quality Polaroid's.
1995	Gatling[152]	n = 59 of 129 patients (6.7%) recalled of 1922 screened.
	Method	Mydriatic direct ophthalmoscopy.
	Professional group	Optometrists in 76 optical practices.
	Reference standard	Nil.
	Outcome measure	Referral to Ophthalmologist, follow-up in diabetic clinic or discharged to annual screening.
	Result	Of the 59 recalls, referral to the Ophthalmologist was made in 15 cases for potentially sight-threatening retinopathy and 14 cases were followed in the diabetic clinic for significant background retinopathy.
1995	Jacob[143]	n = 1050 p.
	Method	Direct and indirect ophthalmoscopy, and single field mydriatic Polaroid photography with the Canon CR3 45 NM camera.
	Professional group	Technician.
	Reference standard	Grading of the Polaroid photographs by a consultant Ophthalmologist.
	Outcome measure	Prevalence of DR and agreement between the technician's findings and the consultant gradings.

	Result	Prevalence of DR of 27%, 14% previously undetected with 0.5% prevalence of STDR. There was almost complete agreement between the technician's findings and the consultant analysis of photographs.
1996	O'Hare[144]	n = 1010 p.
	Method	Adding single 45 degree field Polaroid photographs taken after mydriasis to mydriatic direct ophthalmoscopy.
	Professional group	General practitioners and opticians.
	Reference standard	Mydriatic direct ophthalmoscopy by an Ophthalmologist, combined with review of the Polaroid photographs.
	Outcome measure	Detection of any DR and of referable DR.
	Result	The sensitivity of detecting referable retinopathy by general practitioners improved from 56% to 80% with photographs; for opticians it improved from 75% to 88%.
1998	Gibbins[141]	Welsh Community Diabetic Retinopathy Study.
	Method 1	Direct ophthalmoscopy by GP's, study Optometrist's and community Optometrist's.
	Method 2	2 field mydriatic 45 degree 35mm colour slide retinal images.
	Reference standard	External grading of 35 mm slides.
	Results	For direct ophthalmoscopy, GPs achieved a sensitivity of 65.7%, specificity 93.8% and positive predictive value (PPV) 65.7%. Community Optometrists achieved a sensitivity of 82.2% with a PPV of 50.7%; the study Optometrist 79.2 and 55.9%, respectively.
2003	Namperumal samy[153]	n = 3,949.
	Method	Binocular indirect ophthalmoscopy in 32 screening camps.
	Professional group	Ophthalmologists.

	Reference standard	Nil.
	Outcome measure	Detection of any DR and more severe DR.
	Result	One-fifth of those screened had evidence for any DR; only 6.1% of these persons had evidence of past ophthalmic treatment for retinopathy.
2003	Verma[154]	n = 400 e (of 200 p).
	Method	Mydriatic direct ophthalmoscopy.
	Professional group	General physicians and Optometrists.
	Reference standard	Ophthalmologist's examination using a direct ophthalmoscope.
	Outcome measure	Diagnosis of levels of DR.
	Result	The diagnoses made by the general physician (kappa = 0.8381, SE = 0.041) and the Optometrist (kappa = 0.7186, SE = 0.051) showed good rates of agreement with the Ophthalmologist's diagnoses.

1.2.5.2 Studies of mydriatic photography (< 7 fields) using 35 mm film or Polaroid as a screening method.

In order to compare studies of mydriatic 35 mm or Polaroid photography as a method of screening they have been tabulated below into similar categories and they have been further divided into those that have compared mydriatic 35 mm or Polaroid photography with a recognised reference standard of seven-field stereo photography, an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography, and those that have not.

The studies described below that compared mydriatic 35 mm or Polaroid photography as a method of screening a recognised reference standard show that consistently good results can be achieved using mydriatic photography with 35 mm film or Polaroid in screening for referable or sight-threatening diabetic retinopathy. In those studies reporting sensitivity and specificity Kalm[155], Pugh[138], Harding[139], Taylor[145], Stellingwerf[156], Pandit[157], Olson[158] & Sharp[15] showed > 80% sensitivity for the

detection of sight threatening eye disease or for the detection of any DR. The only one that dropped below 80% was Taylor[145] who found the sensitivity of single 45 degree field Polaroid photography for the detection of any retinopathy 72% (95% CI 66-78%) although for referable retinopathy Polaroid had a sensitivity of 90% (95% CI 86%-94%).

The study described by Backlund[159] did not use a recognised reference standard but described the attendance and presence of levels of DR in 6863 diabetes patients in Stockholm County in Sweden demonstrating the feasibility of this screening method.

In the studies mentioned, specificity does vary depending on whether ungradeable images are regarded as test positive but levels of > 85% are consistently achieved. The high sensitivities for these photographic methods of screening have led to a widespread acceptance of photographic screening for sight-threatening diabetic retinopathy. Some of the unanswered questions are around the effectiveness and cost-effectiveness of digital photography, the use of mydriasis versus non-mydriasis and the number of fields.

Studies comparing mydriatic photography (< 7 fields) using 35 mm film or Polaroid with a recognised reference standard of seven-field stereo photography, an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography:

Year	Author	Number of patients in study (n) patients (p) eyes (e)
1989	Kalm[155]	n = 185 p type II diabetes.
	Methods	Two 45 degree non-stereo 35mm mydriatic fundus photography.
	Reference standard	Estimation of the true prevalence from photography and indirect slit lamp biomicroscopy using a 60D lens by an Ophthalmologist.
	Outcome measure	Detection of BDR, PPDR, PDR and diabetic maculopathy.

	Result	The sensitivity of the photographic method was 87/97% (right eye/left eye) when detecting BDR and 81/80% for maculopathy versus 69/61% and 79/63%, respectively, with the slit-lamp method.
1993	Lee[160]	n = 410 p Oklahoma Indians (795 e).
	Methods	One 45 degree field 35mm non-mydriatic fundus photography through dilated pupils.
	Reference standard	Slit lamp biomicroscopy with a 90 D lens by one of three Ophthalmologists.
	Outcome measure	Diagnosis of no DR, NPDR and PDR.
	Result	Of the 730 eyes that were gradeable by both methods overall agreement between the two methods in diagnosing no retinopathy, non-PDR and PDR was 86.3% with a kappa statistic kappa of 0.74 was found. For the diagnosis of proliferative diabetic retinopathy (PDR), there was an agreement of 98.1% with a kappa of 0.84. With a total of 61 cases of proliferative retinopathy diagnosed by either method in our study, ophthalmoscopy alone detected 88.5% and fundus photography, 78.7%.
1993	Pugh[138]	n = 352 p.
	Methods	Three dilated 45 degrees 35mm retinal photographs.
	Reference standard	7-field stereo-photography.
	Outcome measure	Retinopathy levels were dichotomised into no DR and mild NPDR versus moderate to severe NPDR and PDR.
	Result	Sensitivity of 0.81, specificity of 0.97, positive and negative likelihood ratios of 24 and 0.19.
1993	Schachat[161]	n = 1168 p (history of diabetes in 21%).
	Methods	Two mydriatic 30 degree stereoscopic photographs of the disc and macula.

	Reference standard	Direct ophthalmoscopy and slit lamp biomicroscopy using a 78 dioptre lens, three mirror lens or both by an experienced Ophthalmologist.
	Outcome measure	Detection of any DR.
	Result	The frequency of diabetic retinopathy was 7.7% (90/1168) by clinical examination, 8.7% (102/1168) by photograph grading, and 6.7% (78/1168) by both methods.
1995	Aldington[162]	N = 48 e.
	Methods	2 x 45 degree 35mm retinal photography - macular and nasal fields.
	Reference standard	7-field stereo-photography.
	Outcome measure	Mild background, moderate to severe background and proliferative or photocoagulated.
	Result	In eyes with diabetic retinopathy (n=41), at least one grader (one of five) using the new system matched the verified results in 38 out of 41 (93%) eyes and three or more graders matched in 31 (76%) eyes.
1995	Harding[139]	326 patients with diabetes.
	Methods	Mydriatic three x 45 degree field 35 mm photography.
	Reference standard	Slit-lamp biomicroscopy by a retinal specialist.
	Outcome measure	Detection of sight threatening eye disease.
	Result	Sensitivity of detection of sight threatening eye disease by photography was 89% (CI 80-98%), and specificity was 86% (CI 82% to 90%).
1996	Kiri[163]	n = 123 p (208 e).
	Methods	Mydriatic simultaneous fundus stereo photography (using the Nidek 3Dx camera).

	Reference standard	Slit lamp biomicroscopy with a fundus contact lens (CLBM) by three retina specialists.
	Outcome measure	Detection of clinically significant macular oedema and foveal centre thickening.
	Result	One hundred eighty-four (88%) of the 208 stereo photographs were of sufficient quality to detect clinically significant macular oedema; 175 (84%) of the 208 stereo photographs detected foveal centre thickening. The agreement between the clinician and the photographic grading, measured by weighted kappa, was 0.52 for clinically significant macular oedema and 0.58 for foveal centre thickening.
1999	Taylor[145]	n = 731 (118 reference standard test).
	Methods	Single 45 degree field Polaroid photography.
	Reference standard	7-field stereo-photography.
	Outcome measure	Detection of referable retinopathy.
	Result	For the detection of any retinopathy, Polaroid had a sensitivity of 0.72 (95% CI 0.66-0.78) and for referable retinopathy Polaroid had a sensitivity of 0.90 (95% CI 0.86-0.94). Specificity stated to be not significantly different to digital (0.88 and 0.97 no confidence intervals given).
2000	Broadbent[164]	n = 106 p (106 of the 140 identified patients attended).
	Methods	Mydriatic stereo macular photography in addition to mydriatic three-field 35mm photography.
	Reference standard	Reference standard of slit-lamp biomicroscopy by a retinal specialist.
	Outcome measure	Detection of clinically significant macular oedema.

	Result	78.3% of standard photographs and 75% of stereo photographs were graded as good or fair. CSMO was found in 11 eyes on slit lamp biomicroscopy. In all cases no CSMO was detected on stereo-photography. Every case of CSMO was associated with macular exudates within 1DD of fixation.
2001	Moller[165]	N = 44 e (23 p).
	Methods	One 60 degrees mydriatic 35mm fundus photograph.
	Reference standard	Seven field stereo fundus photography and fluorescein angiography was performed in all patients.
	Outcome measure	Identifying proliferative diabetic retinopathy in eyes with moderate/severe non proliferative diabetic retinopathy.
	Result	In four eyes of three patients (11.1% of eyes) retinal neovascularisation was found. This condition was not found on examination of 60 degrees fundus photographs.
2001	Stellingwerf[156]	n = 469 p.
	Methods	Two mydriatic 45 degrees 35mm photographic fields per eye (macular and nasal).
	Reference standard	Binocular indirect ophthalmoscopy and slit-lamp biomicroscopy by one of six Ophthalmologists.
	Outcome measure	Identifying sight-threatening retinopathy.
	Result	The sensitivity for STDR was 95% (specificity 99%) and for any DR was 83% (specificity 88%). The percentage of referrals to an Ophthalmologist was 6.2%. All patients with macular oedema detected by biomicroscopy were classified as having vision-threatening retinopathy on the photographs.
2002	Pandit[157]	n = 609 (6.4%) of 9468 patients screened.
	Methods	Mydriatic single 45 degree Polaroid retinal photography and direct ophthalmoscopy.
	Reference standard	Slit-lamp biomicroscopy was performed by an SPR in ophthalmology.

	Outcome measure	Detection of STDR.
	Result	The sensitivity and specificity of detection of STDR was 82.5% and 98%, respectively, for the Hospital Screening Programme; 85.7% and 95.7%, respectively, for the District Screening Programme; and 83.3% and 96.8% for both services combined.
2003	Anderson[166]	n = 64 p from 17 nursing homes.
	Purpose	Feasibility of screening for diabetic eye disease in homebound nursing home residents.
	Methods	An Ophthalmologist and nurse performed Bailey-Lovie Logmar visual acuity (VA), portable slit-lamp examination, 35 mm fundus photography.
	Camera	Kowa 6 x 30 degree field.
	Population	A total of 54 (78%) nursing homes responded reporting 199/2427 (8.2%) residents with diabetes. Of these, 64/80 (80%) residents in 17 homes were examined.
	Outcome measure	Screen-positive patients for sight-threatening DR were invited to a dedicated assessment clinic.
	Result	VA possible in 50 (78%); slit-lamp examination in 56 (88%); gradable photographs in at least one eye in 34 (53%); STED in 12 (35%) patients. In all, 35 (70%) patients had Snellen-equivalent VA worse than 6/12 in the better eye, of whom 13 (26%) were worse than 6/60. Of 29 screen positive patients, 12 attended the assessment clinic: one was unable to cooperate outside the home; 11 continue under ophthalmic review, four for previously undetected STED of which one listed for laser photocoagulation.
2003	Olson[158] & Sharp[15]	n = 586.
	Methods	One and two 50 degree field 35mm fundus photography.

	Reference standard	Slit-lamp biomicrocopy by retinal specialists.
	Outcome measure	Any DR, CSMO and STDR.
	Result	For the detection of any DR, 35 mm colour slides – sensitivity of 89% (CI 84-94) and specificity of 89% (CI 86-92). Single macular field only sensitivity of 86% (CI 80-92) and specificity of 92% (CI 88-94). For the detection of STDR, two field 35 mm colour slides – sensitivity of 96% (CI 87-100) and specificity of 89% (CI 86-91). Single macular field only sensitivity of 95% (CI 85-99) and specificity of 89% (CI 86-92). Technical failure rate of colour slide photography (11.9%). For the detection of CSMO, 35 mm colour slides – sensitivity of 83% (CI 61-95) and specificity of 84 %(CI 81-87). In the Sharp[15] report, 10% of patient visits produced one or more ungradeable fields for 35 mm photography. In the Olson[158] report a technical failure rate of colour slide photography was reported as 11.9%.

Studies of mydriatic photography (< 7 fields) using 35 mm film or Polaroid without a recognised reference standard:

1998	Backlund[159]	n = 5490 p.
	Methods	Three-field 35mm fundus photography.
	Reference standard	Nil.
	Outcome measure	Attendance and presence of levels of DR.

	Result	6863 diabetes patients in Stockholm County were invited; 5490(80%) attended. 77% of persons with known diabetes were reached; only 37% had their eyes examined during the preceding 2 years. For 97% of patients, images were assessable. DR was present in 34% of patients (non-proliferative DR not requiring further assessment 29%, non-proliferative DR requiring further assessment 1.1%, proliferative DR 0.5% and macular involvement 2.6%).
1998	Penman[167]	n = 427 p (427 right eyes only).
	Methods	One 45 degree mydriatic 35mm fundus photograph using a non-mydriatic camera through a dilated pupil.
	Reference standard	Binocular indirect ophthalmoscopy performed by three resident Ophthalmologists from the Cairo Institute.
	Outcome measure	Four categories were used for comparison: No DR, STDR, non-STDR and ungradeable.
	Result	Ninety-two (22%) of the 427 retinal photographs were ungradeable; in 58 eyes (63%), this was due to media opacity (42 eyes with cataract, 3 with corneal opacity, and 13 with both). Agreement between retinal photography and indirect ophthalmoscopy was poor (kappa = 0.33; 95% CI = 0.27-0.39) and primarily due to the large number of eyes (n = 79) with ungradeable photographs that could be graded by ophthalmoscopy.
2000	Liesenfeld[168]	n = 129 p.
	Methods	Assessment of digital photographs by six screening centres who received the images by electronic mail.
	Reference standard	Conventional 35-mm transparencies of the same fields as the digital photographs for detection of diabetic retinopathy. Slit-lamp biomicroscopy by the six Ophthalmologists for the detection of macular oedema.
	Outcome measure	Detection of any DR and sight-threatening DR including macular oedema.

	Result	The assessment of digital images by the six screening centres resulted in a median sensitivity of 85% and a median specificity of 90% for the detection of moderate NPDR or STDR (n = 7). Clinically significant macular oedema (n = 4) was correctly identified in 15 of the 24 grading reports.
2003	Agrawal[169]	n = 150 e on 2 occasions total n = 300e.
	Methods	The authors looked at 150 consecutive images in May 2002 and another 150 in September 2002.
	Reference standard	Comparison to the NSC recommendation of < 5%.
	Outcome measure	The technical failure rate (poor quality images).
	Result	The technical failure rate in the completed audit cycle was 7%. In all, there were 13 (4.3%) technical failures due to media opacity, small pupil or difficult positioning of the patient. There were eight technical failures due to photographic error, five in the first audit and three in the second.

1.2.5.3 Studies comparing mydriatic digital photography as a method of screening for diabetic retinopathy.

In order to compare studies of mydriatic digital photography as a method of screening they have been tabulated below into similar categories and they have been further divided into those that have compared mydriatic digital photography with a recognised reference standard of seven-field stereo photography, an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography, and those that have not.

In those studies that compared mydriatic digital photography to a recognised reference standard, those by Newsom[170] and Razvi[171], contained less than 100 patients. Those studies that included more than 100 patients showed the following results:
Taylor[145], using a single 45 degree field mydriatic digital photography found a sensitivity of 74% (95% CI 68-80%) for the detection of any DR, and a sensitivity of 85% (95% CI 80-90%) for the detection of referable retinopathy and specificity 88% and 97% (no confidence intervals given) in 731 patients. However, this study had relatively small numbers of referable retinopathy (20) in their reference standard group of 118. Rudnisky[172] found sensitivity ranging from 50.0% (for detection of CSME 2) to 90.6% (CSME overall) using high-resolution mydriatic 30 degree stereoscopic digital photography. Specificity ranged from 90.0% (macular oedema) to 99.0% (CSME 2). No confidence intervals were given. 207 eyes of 105 patients were included in the study. Olson[158] & Sharp[15] reported that, for the detection of sight-threatening retinopathy, manual grading of two-field red-free digital images achieved a sensitivity of 93% (82-98) and a specificity of 87% (84-90). Single macular field only sensitivity of 93% (CI 83-98) and specificity of 87% (CI 84-90). This study included 586 patients.

In those that did not use a recognised reference standard those by Friberg[173], George[174], George[175] and Shiba[176] contained less than 100 patients and the study by Jensen[177] was designed to test the target resolution of digital cameras against a test target placed in an artificial eye. Those studies that did not use a recognised reference standard that included more than 100 patients showed the following results:
Ryder[178] concluded by side by side comparisons in 213 eyes from 107 patients that electronic imaging was superior to Polaroid at lesion detection. Henricsson[179] found an exact agreement between grades obtained from the colour slides and the digital colour images in 82% (weighted kappa 0.88; 95% CI 0.80-0.96), and in 85% when red free

images were used as an adjunct to the digital colour images. Tennant[180] used Pearson's correlation coefficient for the presence of retinopathy to compare slide film and stereoscopic digital imaging, which was 0.92 for microaneurysms, 0.80 for haemorrhages, 0.45 for intraretinal microvascular abnormalities, 0.32 for venous beading, 1.00 for neovascularisation of the disc, 1.00 for neovascularisation elsewhere in the retina and 0.97 for clinically significant macular oedema ($p < 0.001$). The correlation between the two techniques for severe non proliferative diabetic retinopathy (NPDR) was 0.86 and for high-risk proliferative diabetic retinopathy 1.00 ($p < 0.001$).

Mydriatic digital photography has shown promising results in the above studies for detection of levels of diabetic retinopathy, but none of these studies tested this method in a population based screening environment, which was the subject of the current thesis. The Gloucestershire Diabetic Eye study was designed to assess the use of digital photography as a method of screening for referable diabetic retinopathy in a mobile population screening environment.

Studies comparing mydriatic digital photography with a recognised reference standard of seven-field stereo photography, an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography:

Year	Author	Number of patients in study (n) patients (p) eyes (e)
1999	Taylor[145]	n = 731. 118 had reference standard test.
	Methods	Single 45 degree field mydriatic digital photography using a TopconTRCNW5s with Sony 3-chip CCD camera & Imagenet software and 534 using a Canon CR5-45NM with Sony 3-chip CCD camera and Ris-Lite software.
	Resolution	Topcon 640 x 480 pixels. Canon 768 x 576 pixels.
	Reference standard	7-field stereo-photography.
	Outcome measure	Detection of any DR and referable retinopathy.

	Result	For the detection of any DR, digital photography had a sensitivity of 0.74 (95% CI 0.68-0.80) and for referable retinopathy digital photography had a sensitivity of 0.85 (95% CI 0.80-0.90) and Specificity 0.88 and 0.97 (no confidence intervals given).
2000	Newsom[170]	N = 37 p (73 e).
	Methods	Three 45 degrees mydriatic digital colour photography and a single macula 45 degrees oral fluorescein angiography with a Zeiss FF 450 camera.
	Resolution	Not stated.
	Reference standard	7-field stereo-photography.
	Outcome measure	Detection of any DR and the detection of diabetic maculopathy.
	Result	For grading diabetic retinopathy digital colour photography produced a sensitivity of 0.87 (specificity 0.83); OFA produced a sensitivity of 0.87 (specificity 0.80) ($p = 0.1$). For the detection of diabetic maculopathy, the sensitivity of digital colour photography was 0.48 (specificity of 0.95) and for OFA was 0.87 (specificity 0.87) ($p < 0.01$). No confidence intervals were given.
2001	Razvi[171]	n = 84 p.
	Methods	Oral fluorescein angiography (OFA) using single 30 degree digital imaging at 15, 30, 45 and 60 minutes with a Topcon 50IA camera and Kodak Mega Plus CCD.
	Resolution	1024 x 1024 pixels.
	Reference standard	Ophthalmologist slit lamp biomicroscopy.
	Outcome measure	Detection of clinically significant macular oedema.

	Result	This study indicates a sensitivity of 92% and specificity of 81%. Only 4.8% of patients developed a minor reaction to oral fluorescein; 84.5% of images were of good quality.
2002	Rudnisky[172]	n = 207 e of 105 p.
	Methods	High-resolution mydriatic 30 degree stereoscopic digital photography with Kodak/Canon 9CS560 and Zeiss 30^0 fundus camera. Viewed using liquid crystal shutter goggles.
	Resolution	3040 x 2008 pixels.
	Reference standard	Slit-lamp biomicroscopy with a fundus contact lens (contact lens biomicroscopy - CLBM) by a retina specialist.
	Outcome measure	Presence or absence of the ETDRS criteria for CSME. CSME 1, CSME 2, CSME 3, macular oedema, microaneurysms, intraretinal haemorrhage, and hard exudates.
	Result	Exact agreement was high for all identified pathologic conditions: CSME overall, 83.6%; CSME 1, 83.6%; CSME 2, 96.1%; CSME 3, 88.5%; macular oedema, 75.0%; microaneurysms, 77.9%; intraretinal haemorrhage, 83.7%; and hard exudates, 73.1%. Sensitivity ranged from 50.0% (CSME 2) to 90.6% (CSME overall). Specificity ranged from 90.0% (macular oedema) to 99.0% (CSME 2).
2003	Olson[158] & Sharp[15]	n = 586.
	Methods	One and two-field mydriatic red free digital photography using a Topcon 50X fundus camera with Kodak Mega Plus CCD.
	Resolution	1024 x 1024.
	Reference standard	Slit-lamp biomicrocopy by retinal specialists.

	Outcome measure	Any retinopathy, clinically significant macular oedema and sight-threatening retinopathy (otherwise described as referable).
	Result	For the detection of sight-threatening retinopathy, manual grading of two-field red-free digital images achieved a sensitivity of 93% (82-98) and a specificity of 87% (84-90). Single macular field only sensitivity of 93% (CI 83-98) and specificity of 87% (CI 84-90). Digital imaging had a technical failure rate of 4.4% of patients. For the detection of any retinopathy, manual grading of two-field red-free digital images had a sensitivity of 83% (77-89) and specificity of 79% (75-83). Single macular field only sensitivity of 80% (CI 74-86) and specificity of 88% (CI 84-91). For the detection of clinically significant macular oedema, manual grading of two-field red-free digital images had a sensitivity of 83% (61-95) and specificity of 83% (80-86).

Studies of mydriatic digital photography without a recognised reference standard:

Year	**Author**	**Number of patients in study (n) patients (p) eyes (e)**
1987	Friberg[173]	n = 50.
	Methods	Digital fundus and fluorescein angiographic images with a Panasonic WV/850 for black and white and JVC KY1900 CH for colour.
	Resolution	512 x 512 pixels.
	Reference standard	35 mm photographs.
	Outcome measure	Retinal features.
	Result	Compares well with images from 35 mm film.
1998	George[174]	N = 75 e.

	Methods	2 field mydriatic 45 degree digital retinal images using a Canon CR5.
	Resolution	785 x 576 pixels.
	Reference standard	2 field mydriatic 45 degree 35 mm colour transparencies using a Canon CR5.
	Outcome measure	Detecting any DR and grade of diabetic retinopathy.
	Result	There was exact agreement between grades obtained from both the 2 field 45 degrees 35 mm colour transparencies and digital images in 93.3% (70/75) of eyes, with a Kappa of 0.92.
1998	Ryder[178]	N = 213 from 107 p.
	Methods	One 45 degree field mydriatic digital image using a Canon CR5 45NM with Sony DXC 930 3-chip video camera.
	Resolution	Not stated.
	Reference standard	One 45 degree field mydriatic Polaroid retinal photography.
	Outcome measure	Detection of any DR and referable DR.
	Result	Of 34 eyes requiring Ophthalmologist referral according to standard European criteria, 34/34 (100%) were detected on the electronic image and only 24/34 (71%) on the Polaroid. Side by side comparisons showed electronic imaging to be superior to Polaroid at lesion detection.
1999	Jensen[177]	
	Methods	Study of the resolution of retinal digital colour images.
	Resolution	The diameter of the circular field of the diaphragm gave a pixel dimension of 1464 pixels for Kodak DCS420, 2900 pixels for Kodak DCS460 and 1760 pixels for Color Crisp Carnival 2000.
	Reference standard	A test target placed in an artificial eye.

	Outcome measure	Target resolution.
	Result	The maximal target resolution of the fundus camera was 6 micrometers corresponding to 24 micrometers at the image plane. The best film material matched this closely. The size of the digital image must be 2-3000 pixels to match this resolution. This criterion is fulfilled by present high-end digital cameras.
1999	George[175]	n = 150 e.
	Methods	150 macula centred retinal images were taken as 35 mm colour transparencies representing a spectrum of diabetic retinopathy, digitised, and graded in random order before and after the application of a sharpen filter (Adobe Photoshop). Digital enhancement of contrast and brightness was performed and an X2 digital zoom was utilised.
	Resolution	768 x 512 pixels.
	Reference standard	Grading of 35 mm colour transparencies.
	Outcome measure	Detection of retinopathy grades.
	Result	Overall agreement in retinopathy grade from the digitised images improved from 83.3% (125/150) to 94.0% (141/150) with sight threatening diabetic retinopathy (STDR) correctly identified in 95.5% (84/88) and 98.9% (87/88) of cases when using unenhanced and enhanced images respectively.
2000	Henricsson[179]	n = 283.
	Methods	Comparative study of 4 x 50-degree mydriatic digital images (fields 1-3 of the seven standard fields and stereo-pairs of the macula) using Topcon TRC50 with Sony DXC 930.
	Resolution	800 x 600 pixels.

	Reference standard	4 x 50 degree 35mm slides (same fields).
	Outcome measure	Grading result of the worst eye (according to the Wisconsin classification) by an Ophthalmologist and ophthalmic nurse independently.
	Result	There was exact agreement between grades obtained from the colour slides and the digital colour images in 82% (weighted kappa 0.88; 95% CI 0.80-0.96), and in 85% when red free images were used as an adjunct to the digital colour images. Inter- and intra-grader agreement (weighted kappa) varied between 0.77 and 0.84 for digital photography and between 0.88 and 0.90 for colour slides.
2001	Tennant[180]	n = 121 p (241 e) 47.1% with DR.
	Methods	Mydriatic seven 30 degree field digital imaging (with stereo pairs of fields 1 and 2 - macula and disc) with Kodak DCS560 and Zeiss fundus camera.
	Resolution	2008 x 3040 pixels.
	Reference standard	35 mm slide photography taking the same fields.
	Outcome measure	The detection of different features of diabetic retinopathy.
	Result	Pearson's correlation coefficient for the presence of retinopathy between slide film and stereoscopic digital imaging was 0.92 for microaneurysms, 0.80 for haemorrhages, 0.45 for intraretinal microvascular abnormalities, 0.32 for venous beading, 1.00 for neovascularisation of the disc, 1.00 for neovascularisation elsewhere in the retina and 0.97 for clinically significant macular oedema ($p < 0.001$). The correlation between the two techniques for severe non proliferative diabetic retinopathy (NPDR) was 0.86 and for high-risk proliferative diabetic retinopathy 1.00 ($p < 0.001$).
2002	Shiba[176]	n = 94.

Methods	Nine overlapping 45 degrees fundus photographs with and without mydriasis using Topcon TRCNW5s with Sony DXC-970 3CCD colour camera.
Resolution	Not stated.
Reference standard	Ophthalmologist examination -only states in the article ophthalmoscopy.
Outcome measure	Severity of DR levels – No DR, very mild NPDR, mild NPDR, moderate NPDR, severe NPDR, PDR.
Result	For 9 field collage and for 3x3 edited forms, sensitivity for the presence of DR is 82% and specificity 100%. No confidence intervals given.

1.2.5.4 Studies of non-mydriatic photography.

In order to compare studies of non-mydriatic photography as a method of screening they have been tabulated below into similar categories and they have been further divided into those that have compared non-mydriatic photography with a recognised reference standard of seven-field stereo photography, an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography, and those that have not.

The use of non-mydriatic photography has been reported from the USA[138 181-183], Japan[176], Australia[184 185], France[186], and the UK[187-191].

Five studies have included a recognised reference standard and have reported sensitivity and specificity of the method. They have been reported by Pugh[138], Bursell[182], Lin[183], Herbert[192] and Massin[186].

Pugh[138] reported a sensitivity and specificity for detection of none and mild NPDR versus mod to severe NPDR & PDR for non-mydriatic photography of 61% and 85%. The ungradeable image rates reported was 14%. The study by Bursell[182] only included 108 eyes of 54 patients with mean age of 48 yrs. No confidence intervals were given. The study by Lin[183] excluded 197 patients (48.5%) for unusable seven-field reference standard photos and a further 12 patients (2.96%) because of unusable ophthalmoscopy records, and which made it difficult to interpret the ungradable image rate of 8.1% in the remaining patients in the study. No confidence intervals were given for the sensitivity and specificity results. Herbert[192] compared one 45^0 field digital images from a non-mydriatic Topcon TRC-NW5s i/c Sony 3-chip video camera without mydriasis (except in those with blurred images when mydriasis was performed) with a reference standard of slit-lamp bio-microscopy by a retinal specialist in 301 eyes. The sensitivity for detection of any DR was 38% and specificity 95% after exclusion of ungradeable images. No confidence intervals were given. Massin[186] compared five 45^0 field non-mydriatic colour digital photography (without dilation) using a Topcon TRC-NW6s i/c Sony DXC-950p video with a reference standard of 7-field stereophotography in 147 eyes of 74 patients. Sixteen eyes of nine patients (11%) were judged ungradeable by at least one observer. Results showed that the sensitivities of detection for moderately severe to severe DR, reported by the three observers were 92, 100 and 92%, respectively, and the specificities, 87, 85, and 88%. No confidence intervals were given. If ungradable image rates are included as test positive this influences the sensitivity and specificity results. Reports of ungradable image rates for non-mydriatic photography vary between 4% reported by Leese[188] and 34% reported by Higgs[191].

In the first report of non-mydriatic photography in 1985 using a Topcon TRC NW2, Klein[193] reported that, of the 99 photos taken with the non-mydriatic camera, 36 were lost due to a malfunction of flash syncronisation of the camera. Of the remaining 63, 12.7% (8 of 63) were considered ungradable. The authors commented that it took longer to take photos with the non-mydriatic camera through an undilated pupil in older persons (> 60 yrs vs. < 60 yrs) with dark iris colour and media opacities.
From the other studies the possible factors that have been suggested that might have an influence on image quality in non-mydriatic retinal photography are:

1. Age – suggested in the following studies
   a) Higgs[191] reported that 13% < 50 years, 39% 50-70 yrs, and 54% > 70 years had ungradable images.
   b) Buxton[140] reported that the ungradable image rate varied between 2% in the Exeter physician group to 9% in the Oxford GP group. The difference between these two groups was that age varied from 49 $\pm$ 18 in the Exeter physician group to the age in the Oxford GP group was 61 $\pm$ 15. Other differences between these two groups were that duration of diabetes varied from 11 $\pm$ 10 in Exeter physician group to 7 $\pm$ 7 in the Oxford GP group. The proportion of IDDM varied from 75% in the Exeter physician group to 21% Oxford GP group.
   c) Some studies[182 186] have reported ungradable image rates < 12% but the average age of the study population was under 55 years.
2. Duration of diabetes – this is suggested by a study by Cahill[194] in 2001, in which it was reported that pupillary autonomic denervation increases with increasing duration of diabetes mellitus.
3. Ethnicity – suggested in the Klein[193] study.
4. Flash intensity - Taylor[145] reported less patient discomfort with the lower flash power (10 W vs. 300 W) of the digital system compared to the Polaroid system. When used in non-mydriatic photography, there is a faster pupil recovery time with lower flash intensities, which may improve image quality in nasal images and/or those from the fellow eye.

Age, duration of diabetes and ethnicity were not reported in some studies[185 189 195], others[138 184] have reported these variables but have not reported an association. Shiba[176] excluded the over 70 years age group and remarkably attempted 9 x overlapping non-

mydriatic 45^0 fields[176], whereas other studies have only attempted five-fields[186], 3-fields[181 182] and the majority only one non-mydriatic field[138 140 184 187 188 191]. Assessment of ungradable images uses subjective criteria with varying definitions used by different studies. Patient numbers varied between studies from 40 eyes in the study by Lim[181] to 3611 patients in the current study.

The Gloucestershire Diabetic Eye study was designed to formally evaluate the introduction of a community based non-mydriatic and mydriatic digital photographic screening programme that was introduced in October 1998 and to evaluate the effect of age and duration of diabetes on the image quality in non-mydriatic and mydriatic digital photographic screening.

Studies comparing non-mydriatic photography with a recognised reference standard of seven-field stereo photography, an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography:

Year	Author	Number of patients in study (n) patients (p) eyes (e)
1988	Jones[189]	n = 127 eyes.
	Type of non-mydriatic photography	One 45 degree field Polaroid colour.
	Camera	Canon CR3.
	Type of mydriatic photography	One 45 degree field 35 mm colour.
	Reference standard	6 x 30 degree 35mm fluorescein.
	Ungradeable reference standard photos	Not reported.
	Outcome measure	The detection of DR - microaneurysms, haemorrhages, and hard and soft (cotton wool spots) exudates and new vessels.

	Results	The detection of DR was equivalent for Polaroid prints and 35 mm transparencies of equivalent quality. The image quality was unassessable in almost 1 in 5 and in two cases with disc new vessels; these were not seen on the Polaroid prints.
	Age	Not reported.
	Gender	Not reported.
	Ethnicity data	Not reported.
	Duration of diabetes	Not reported.
	IDDM & NIDDM	Not reported.
	Ungradeable images	Almost one in five (22/127) Polaroid prints could not be assessed owing to poor quality compared with 3 (2.4%) 35 mm transparencies.
1993	Pugh[138]	N = 352 .
	Type of non-mydriatic photography	One 45 degree field 35mm colour.
	Camera	Canon CR3.
	Type of mydriatic photography	3 x 45 degree field 35 mm colour.
	Reference standard	7-field stereo 35mm.
	Ungradeable reference standard photos	1 had ungradeable reference standard photos in both eyes.
	Method of calculation of sensitivity and specificity	The worst eye on the reference standard was used in the analysis.
	Outcome measure	None and mild MPDR versus mod to severe NPDR and PDR.

	Results	Sensitivity and specificity and positive and negative likelihood ratios were: photographs without pharmacological dilation 0.61, 0.85, 4.1, 0.46 and dilated photographs 0.81, 0.97, 24, 0.19.
	Age	59% < 65 yrs old.
	Gender	76% male.
	Ethnicity data	52.1% were non-Hispanic white, 10.3% African American, and 37.6% Mexican American.
	Duration of diabetes	Mean was 9.8 years.
	IDDM & NIDDM	5 IDDM, 247 NIDDM.
	Ungradeable images	Non-mydriatic 14%, mydriatic 3.7%.
2001	Bursell[182]	n = 54 p (108 e).
	Type of non-mydriatic photography	3 x 45 degree field digital-video.
	Camera	Topcon TRNW5s i/c Sony 970 video and JVN software.
	Resolution	640 x 480 pixels.
	Reference standard	Seven-field stereo 35mm.
	Ungradeable reference standard photos	None reported.
	Method of calculation of sensitivity and specificity	Not clear.

Outcome measure	Sensitivity and specificity results were given by ETDRS retinopathy level and by lesion but no confidence intervals were given. Timing of next ophthalmic evaluation and prompt referral to an Ophthalmologist. The clinical level of diabetic retinopathy was assessed by macular thickening within 3000 microns of the centre of the macula.
Results	No DR sensitivity 0.76 and specificity 0.94, mild DR sensitivity 0.59 and specificity 0.80, moderate NPDR sensitivity 0.59 and specificity 0.89, severe NPDR sensitivity 0.46 and specificity 0.97, very severe NPDR sensitivity 0.99 and specificity 0.80, PDR < HRC sensitivity 0.89 and specificity 0.97, PDR > HRC sensitivity 1.00 and specificity 1.00.
Kappa values	Kappa for macular oedema was 0.46 $\pm$ 0.06. For no DR k = 0.78 + 0.07, mild DR proliferative with high risk k = 0.31 $\pm$ 0.03, moderate NPDR k = 0.49 $\pm$ 0.04, severe NPDR k = 0.50 $\pm$ 0.06, very severe NPDR k = 0.50 $\pm$ 0.05, proliferative with high risk k = 0.85 $\pm$ 0.09. It also stated that there was substantial agreement (kappa = 0.65 $\pm$ 0.03) between the clinical level of diabetic retinopathy assessed from the undilated JVN images and the dilated ETDRS photos (see outcome measures). The abstract stated agreement was excellent (kappa = 0.87) for suggested referral to ophthalmology specialists for eye examinations but I could not locate this in the results section. The kappa value for macula oedema referral was 0.70 $\pm$ 0.06.
Age	Mean 48 yrs (range 20-75).
Gender	57% male.
Ethnicity data	81.4% white persons, 9.3% African-American, 7.4% Hispanic, 1.9% Asian American.

	Duration of diabetes	Mean 17.7 years ($\pm$ 9.3 yrs).
	IDDM & NIDDM	52% presumed type 1.
	Ungradeable images	11.1% of macular oedema could not be graded because of reduced stereo quality.
2002	Lin[183]	n = 406 p (197 remained for analysis after exclusions).
	Type of non-mydriatic photography	Single 45 degree field digital monochromatic.
	Camera	Canon CR5 i/c software from Ophthalmic Imaging Systems.
	Resolution	640 x 480 pixels.
	Reference standard	Seven field stereo 35mm.
	Unusable reference standard photos	197 patients (48.5%) were excluded for unusable seven-field photos. No explanation was given.
	Other patients excluded	A further 12 patients were excluded from the study because of unusable ophthalmoscopy records.
	Method of calculation of sensitivity and specificity	Including the patients with ungradeable images (16 patients) as a positive test result because in the referral group.
	Outcome measure	The sensitivity and specificity of the methods were compared based on a threshold for referral to further ophthalmologic evaluation (ETDRS level > or =35).
	Results	Sensitivity of digital photos 78%, specificity 86%.
	Kappa values	Kappa = 0.97, P =.0001.
	Age	All > 21yrs, 55% < 59 yrs.
	Gender	Male 58%.
	Ethnicity data	African American 53%, Caucasian American 23%, Asian American 15%, Hispanic 7%, Other 3%.

	Duration of diabetes	Not recorded.
	IDDM & NIDDM	States both but not recorded.
	Ungradeable images	8.1% (16 of the 197 remaining after excluded seven-field and unusable ophthalmoscopy records).
2003	Herbert[192]	n = 301 e, 288 e (145 p) remaining after ungradeable images excluded.
	Type of non-mydriatic photography	One 45 degree field digital images from a non-mydriatic camera without mydriasis (except in those with blurred images when mydriasis was performed). Images compressed to JPEG before grading.
	Camera	Topcon TRC-NW5s i/c Sony 3-chip video.
	Resolution	800 x 600 pixels.
	Reference standard	Slit-lamp biomicroscopy by a retinal specialist.
	Ungradeable reference standard	Nil reported.
	Method of calculation of sensitivity and specificity	After exclusion of ungradeable images.
	Outcome measure	Detection of any diabetic retinopathy.
	Results	The sensitivity was 38% and specificity 95%. No confidence intervals given.
	Age	Not reported.
	Gender	Not reported.
	Ethnicity data	Not reported.
	Duration of diabetes	Not reported.
	IDDM & NIDDM	27% Type 1, 73% Type 2.
	Ungradeable images	4% of eyes screened.

	Comments	There were 42/288 false negatives and 10/288 false positives. Three eyes in the false-negative group (1% of total eyes) had sight-threatening retinopathy requiring laser treatment.
2003	Massin[186]	n = 147 e (of 74 p).
	Type of non-mydriatic photography	Five 45 degree field non-mydriatic colour digital photography (without dilation).
	Camera	Topcon TRC-NW6s i/c Sony DXC-950p video.
	Resolution	800 x 600 pixels.
	Reference standard	Seven field stereo 35mm.
	Ungradeable reference standard	7 patients excluded due to 'poor compliance' and a further 3 ungradeable.
	Method of calculation of sensitivity and specificity	Ungradeable photographs were counted as test positive as they require referral. There were 16 with moderate NPDR or more severe and 12 with CSMO from the reference standard result.
	Outcome measure	The level of retinopathy was dichotomised into Negative – No DR or mild NPDR, Positive – Moderate NPDR or more severe and/or macular oedema or an ungradeable image.
	Results	The sensitivities of detection for moderately severe to severe DR, reported by the three observers were 92, 100 and 92%, respectively, and the specificities, 87, 85, and 88%. No confidence intervals were given.
	Kappa values	For four levels of DR severity (none or mild NPDR, moderate NPDR, severe NPDR and proliferative DR), the percentages of exact agreement between the three observers on the retinopathy grades assigned to the non-mydriatic photographs and to the ETDRS reference slides were 94.6, 93 and 87.6%, respectively (kappa 0.60-0.80).

Age	Mean age 52 yrs.
Gender	46 male, 28 female.
Ethnicity data	Not reported.
Duration of diabetes	Not reported.
IDDM & NIDDM	11 Type 1, 63 Type 2 (of these 54 non-insulin and 9 insulin requiring).
Ungradeable images	Sixteen eyes of nine patients (11%) were judged ungradeable by at least one observer.

Comparative studies of non-mydriatic photography without recognised reference standard.

One relevant study by Cahill[194] on autonomic pupillary changes in type I and II diabetic patients has been included in this section:

Year	Author	Number of patients in study (n) patients (p) eyes (e)
1985	Klein[193]	n = 99 p (with 99 e).
	Type of non-mydriatic photography	1 x 45 degree field non-mydriatic non stereoscopic 35mm retinal photograph.
	Camera	Topcon TRC NW2.
	Type of mydriatic photography	1 x 45 degree field mydriatic non stereoscopic 35mm retinal photograph.
	Reference standard	3 x 30 degree field mydriatic stereoscopic colour photographs of DRS fields 1, 2 and 4 (modified).
	Ungradeable reference standard	2 of 63.
	Other patients not included	Of the 99 photos taken with the non-mydriatic camera, 36 were lost due to a malfunction of flash syncronisation of the camera.

	Outcome measure	Four levels of severity of retinopathy - none, microaneurysms only, all other non proliferative retinopathy and proliferative retinopathy.
	Results	For exact agreement between gradings of retinopathy of the non-mydriatic 45 degrees photographs and the reference standard photos was 82.5% (n = 63); and for mydriatic 45 degrees photographs and the reference standard photos it was 86.5% (n = 74).
	Age	median 54 (15-84 yr).
	Gender	55 male, 44 female.
	Ethnicity data	Not reported.
	Duration of diabetes	Not reported.
	IDDM & NIDDM	Not reported.
	Ungradeable images	Of the remaining 63, 12.7% (8 of 63) were considered ungradeable.
	Comments	It took longer to take photos with the non-mydriatic camera through an undilated pupil in older persons (> 60 yrs vs. < 60 yrs) with dark iris colour and media opacities.
1985	Ryder[196]	2 groups n = 137 e and n = 90 e.
	Type of non-mydriatic photography	1 x 45 degree field Polaroid non-mydriatic retinal photography.
	Camera	137 eyes with CR2 NM and 90 with CR3 NM.
	Reference standard	None.
	Outcome measure	Detection of DR.
	Results	The detection rate of the camera was more than four times higher than that of direct ophthalmoscopy through undilated pupils and more than twice as high as that of direct ophthalmoscopy through dilated pupils.

	Age	Not reported.
	Gender	Not reported.
	Ethnicity data	Not reported.
	Duration of diabetes	Not reported.
	IDDM & NIDDM	Not reported.
	Ungradeable images	22% with CR2 NM and 6% with CR3 NM.
	Comments	Ophthalmoscopy missed circinate rings of exudates encroaching on macula.
1986	Williams[195]	n = 120 e (62 p).
	Type of non-mydriatic photography	1 x 45 degree field non-mydriatic Polaroid or 35 mm retinal photography (86 x Polaroid vs. 34 x 35mm slides).
	Camera	Kowa or Canon CR3.
	Reference standard	Ophthalmologist's examination using direct and binocular indirect ophthalmoscopy.
	Ungradeable reference standard	Not reported.
	Method of calculation of sensitivity and specificity	After exclusion of ungradeable photos.
	Outcome measure	Any DR, maculopathy neovascularisation.
	Results	Sensitivity for detection of any DR of 96%, specificity of 98% with a false negative rate of 6.8% and a false positive rate of 2%. Sensitivity for detection of maculopathy (32 eyes) of 100%, specificity of 96%. Sensitivity for detection of neovascularisation (11 eyes) of 82% (9 detected), specificity of 100%.
	Age	Not reported.
	Gender	Not reported.

	Ethnicity data	Not reported.
	Duration of diabetes	Not reported.
	IDDM & NIDDM	Not reported.
	Ungradeable images	7 eyes.
	Comments	This study did not show any clear advantage of 35mm film or Polaroid.
1990	Rogers[197]	n = 84 p (168 e).
	Type of non-mydriatic photography	1 x 45 degree field non-mydriatic Polaroid retinal photography (95 % undilated, 5% dilated).
	Purpose	Offering a screening service using non-mydriatic Polaroid retinal photography to patients cared for by 27 general practitioners providing diabetes care in their practices.
	Camera	Canon CR3.
	Reference standard	Nil.
	Outcome measure	Detection of any DR.
	Results	Of 84 patients photographed, 26% (22 patients) had appearances of diabetic retinopathy.
	Age	Not reported.
	Gender	Not reported.
	Ethnicity data	Not reported.
	Duration of diabetes	Not reported.
	IDDM & NIDDM	Not reported.
	Ungradeable images	11.9% (20 eyes) after 5% had been dilated.
	Comments	In only seven of 11 patients with maculopathy or proliferative retinopathy had this been detected by their GP by direct ophthalmoscopy.

1990	Taylor[198]	n = 2159 p from the Outpatient diabetic clinics of six hospital diabetic clinics.
	Type of non-mydriatic photography	1 x 45 degree field non-mydriatic Polaroid retinal photography.
	Camera	Canon CR3.
	Reference standard	Nil.
	Other patients not included	Those registered as blind or those in wheelchairs and unable to enter the screening vehicle.
	Outcome measure	Any outcomes of referral to an Ophthalmologist by either method were recorded. Referral for new vessels, pre-proliferative DR, exudative maculopathy, presence of lesions < 1DD from central macula.
	Results	Maculopathy was reported in 147 eyes with camera screening alone and 95 eyes by ophthalmoscopy only (chi 2 = 11.2; p less than 0.001), in 66 and 29 of which respectively maculopathy was subsequently confirmed. Overall, 38 eyes received laser treatment for maculopathy after detection by camera screening compared with 17 after ophthalmoscopic detection (chi 2 = 8.0; p less than 0.01).
	Inter & intra - observer variability	8 QA films were inserted into batches for reporting 5 times by each observer. The mean intra-observer consistency of counting lesions to within 1 band (<1, 2-5, 6-10, 11-20, and >21) was 89.2% for haems, 90.8% for hard exudates and 80% for ma's.
	Age	Range 12-89 yrs.
	Gender	Not reported.
	Ethnicity data	Mostly white.
	Duration of diabetes	0-60 yrs.
	IDDM & NIDDM	Not reported.

	Ungradeable images	Not reported.
	Comments	40 eyes with definite new vessels were detected. Camera screening missed two cases of new vessel formation and did not identify a further 12 but indicated a need for referral. Ophthalmoscopy missed five cases of new vessel formation and indicated a need for referral in another four for other reasons.
1991	Buxton[140]	n = 3318p.
	Type of non-mydriatic photography	1 x 45 degree field non-mydriatic Polaroid retinal photography.
	Camera	Canon camera.
	Reference standard	Mydriatic direct ophthalmoscopy by an ophthalmological clinical assistant.
	Exclusions from study	n = 3318 diabetic patients of 7098 identified. Commonest reason for exclusion was failure to see an Ophthalmologist within the last year.
	Outcome measure	Referral for sight-threatening DR (definition given in the article).
	Results	The performance of the non-mydriatic camera ranged from a sensitivity of 0.35 (CI 0.16- 0.53), with a specificity of 0.95 (CI 0.93- 0.97), with a positive predictive value of 0.29 and negative predictive value of 0.96 in the Oxford GP group. This compared to a sensitivity of 0.67 (CI 0.50- 0.84), with a specificity of 0.97 (CI 0.96- 0.99) with a positive predictive value of 0.67 and negative predictive value of 0.97 in the Exeter physician group.
	Age	Varied from 49 $\pm$ 18 in the Exeter physician group to 66 $\pm$ 13 in the Exeter GP group and the age in the Oxford GP group was 61 $\pm$ 15.

	Gender	Varied from 51% and 52% male in Oxford optician and GP group to 59% male in Exeter GP group.
	Ethnicity data	Not reported.
	Duration of diabetes	Varied from 7 ± 6 Sheffield GP group, 7 ± 7 Oxford GP group to 11 ± 10 in Exeter physician group.
	IDDM & NIDDM	Varied from 5% Sheffield GP group, 21% Oxford GP group to 75% in Exeter physician group.
	Ungradeable images	Varied from 2% in the Exeter physician group to 9% in the Oxford GP group.
1991	Higgs[191]	n = 340 p.
	Type of non-mydriatic photography	1 x 45 degree field non-mydriatic 35mm retinal photography.
	Camera	Canon CR3 NM.
	Reference standard	Nil.
	Other patients not included	358 patients – photographed 340 patients. Camera malfunction 11 patients. Inability to have photos taken 7 patients.
	Outcome measure	Prevalence of any DR and sight-threatening diabetic retinopathy.
	Results	Retinopathy was demonstrated in 124/358 (35%) of patients screened. 48 patients (13%) were judged to have sight-threatening retinopathy, of which 29 patients (8% of the total) were not already under the care of an Ophthalmologist.
	Age	Mean 60 yrs (range 6-89 yrs) 57% > 60 yrs.
	Gender	Not reported.
	Ethnicity data	Not reported.
	Duration of diabetes	Mean 11 yrs (range 0-58 yrs).
	IDDM & NIDDM	29% IDDM.

	Ungradeable images	In only 66% of patients were photographs of both eyes of adequate quality to assess for retinopathy. 34% of patients in one or both eyes (25% of eyes) had ungradeable images. 13% < 50 years, 39% 50-70 yrs, and 54% > 70 years had ungradeable images.
1993	Leese[188]	n = 2984 p (1225 in urban area, 961 in rural area).
	Type of non-mydriatic photography	1 x 45 degree field non-mydriatic Polaroid retinal photography.
	Camera	Canon CR4 NM.
	Reference standard	Nil.
	Outcome measure	Grade of DR (none, background or advanced), need for laser photocoagulation, attendance at a hospital based diabetic clinic, likelihood of receiving insulin.
	Results	Compared with diabetic patients in urban areas, those in rural areas were less likely to attend a hospital based diabetic clinic (46% (442) v 86% (1054), p < 0.001). They were less likely to be receiving insulin (260 (27%) v 416 (34%), p < 0.001. After correction for differences in age distribution, they were more likely to have advanced (maculopathy or proliferative retinopathy) diabetic retinopathy (13% (122) v 7% (89), p < 0.001). They were also more likely to require urgent laser photocoagulation for previously unrecognised retinopathy (1.4% (13) v 0.5% (6), p < 0.02).
	Age	> 60 yrs 65.2% rural, > 60 yrs 58.1% urban.
	Gender	Not reported.
	Ethnicity data	Not reported.
	Duration of diabetes	1-4 yrs 47.3% rural, 1-4 yrs 45.7% urban, 5-9 yrs 24.0% rural, 5-9 yrs 26.3% urban.
	IDDM & NIDDM	IDDM 27% rural, IDDM 34% urban.

	Ungradeable images	4%.
1994	Kiely[199]	n = 433, 268 of these were already being screened. For 165 patients this was the only screening method employed.
	Type of non-mydriatic photography	1 x 45 degree field non-mydriatic Polaroid retinal photography.
	Camera	Not stated.
	Reference standard	Nil.
	Outcome measure	Detection of referable DR.
	Results	Of the 433 patients screened, 39 cases of advanced retinopathy were detected. 23 of these were already known to the eye clinic and only 3 were not attending elsewhere for regular fundoscopy.
	Age	Not reported.
	Gender	Not reported.
	Ethnicity data	Not reported.
	Duration of diabetes	Not reported.
	IDDM & NIDDM	Not reported.
	Ungradeable images	In 58% of patients (n=96) for whom this was the only screening method employed, the photographs were considered substandard (67 patients) or unreadable (29 patients).
1997	Young[200]	
	Type of non-mydriatic photography	Canon CR5 45NM non-mydriatic retinal digital imaging system with the Frost Medical Software RIS-Lite.
	Comments	This was a descriptive article suggesting that digital photography had potential for remote diagnosis and telemedicine.

2000	Constable[201] and Yogesan[185]	49 e of 25 p.
	Type of non-mydriatic photography	1 x ? degree field non-mydriatic digital retinal photography. The angle of photography is not given in the article.
	Camera	Nidek NK NM100 (hand held camera).
	Resolution	640 x 480 compressed to the lowest compression setting on the camera.
	Reference standard	1 x presumed 30 degree field 35mm mydriatic photography using a Zeiss FF fundus camera.
	Ungradeable reference standard	7% of 35mm photos.
	Outcome measure	Identification of levels of DR – microaneurysm, blot haemorrhage, hard exudates, cotton wool spots, NVD, NVE, fibrous tissue, and laser scars.
	Results	Overall agreement between the photographs and digital images was poor (kappa < 0.30).
	Age	Not reported.
	Gender	Not reported.
	Ethnicity data	Not reported.
	Duration of diabetes	Not reported.
	IDDM & NIDDM	Not reported.
	Ungradeable images	16% unacceptable quality. On average, only 24% of the digital images were graded as being good quality and 53% as having an acceptable quality. The remaining 7% had ungradeable reference standard photos. However, 93% of the 35mm photographs were graded as good-quality images for diagnosis.
2000	Lim[181]	n = 40 e (of 22 p).

Type of non-mydriatic photography	3 x 45 degree field non-mydriatic digital photography of three areas: posterior pole, nasal retina, and temporal retina.
Camera	Canon CR6-45NM with Sony DXC-970MD digital back.
Resolution	640 x 480 pixels.
Reference standard	3 x 45 degree field mydriatic 35mm photography of three areas: posterior pole, nasal retina, and temporal retina.
Ungradeable reference standard	3 eyes due to vitreous haemorrhage.
Outcome measure	Presence or absence of neovascularisation of the disc (NVD), neovascularisation elsewhere (NVE), venous beading (VB), nerve fibre layer (NFL) haemorrhage, dot-blot haemorrhage, microaneurysm (MA), clinically significant macular oedema (CSMO), cotton wool spot, intraretinal microvascular anomaly (IRMA), hard exudates (HE), and retinal pigment epithelial (RPE) pigmentary changes.
Results	Sensitivity ranged from 25% (NVD) to 100% (VB). Specificity ranged from 90% (RPE pigmentary changes) to 100% (NVD, NVE, VB, NFL haemorrhage, HE). Positive predictive value ranged from 50% (IRMA) to 100% (NVD, NVE, HE, NFL, VB). Negative predictive value ranged from 48% (MA) to 100% (IRMA).
Kappa values	The kappa value ranged from less than 0.4 for NVD, CSMO, MA, and from 0.4 to 0.7 for NVE, CWS, NFL, dot-blot haemorrhage, VB, IRMA and HE.
Age	Median 60 yrs (range 33-88 yrs).
Gender	Not reported.
Ethnicity data	Not reported.

	Duration of diabetes	Not reported.
	IDDM & NIDDM	Not reported.
	Ungradeable images	3 eyes due to vitreous haemorrhage (same as reference photos).
	Comments	Grading of the non- mydriatic digital images only detected 2 out of the 8 neovascularisation of the disc (NVD), 2 out of the 7 neovascularisation elsewhere (NVE) and 2 out of the 6 eyes with clinically significant macular oedema that were detected by the mydriatic 35 mm slides.
2001	Cahill[194]	72 type I and 69 type II diabetic patients were compared with 120 age matched controls.
	Outcome measure	Mean dark adapted pupil size, mean percentage dilatation in response to cocaine, mean percentage constriction in response to dilute pilocarpine and Valsalva ratio.
	Results	The results suggested that pupillary autonomic denervation occurs before cardiovascular autonomic changes and increases with increasing duration of diabetes mellitus.
2002	Shiba[176]	n = 94 p (separate adolescent study not having reference examination in 66 young people).
	Type of non-mydriatic photography	9 x overlapping 45 degree fundus photographs without mydriasis.
	Camera	Topcon TRC-NW5s Sony DXC-970 video.
	Resolution	Not stated.
	Type of mydriatic photography	9 x overlapping 45 degrees fundus photographs with mydriasis.
	Reference standard	Ophthalmologist's 'ophthalmoscopy'.

Ungradeable reference standard	Not reported.
Other patients not included	Excluded those > 70 yrs.
Outcome measure	Severity of DR levels – No DR, very mild NPDR, mild NPDR, moderate NPDR, severe NPDR, PDR.
Results	For 9 field collage and for 3x3 edited form sensitivity for the presence of DR is 77.6% and specificity 82.1%. The mean grading score evaluated by the conventional non-mydriatic single field was significantly lower than the scores evaluated by the other examination methods ($p < 0.001$) with sensitivity 64.1%, specificity 96.4%. No confidence intervals given.
Age	Adult study 56 ± 8yrs range 39-70 years.
Gender	Adult study 84 male 10 female.
Ethnicity data	Not reported.
Duration of diabetes	14 ± 11yrs.
IDDM & NIDDM	Adult study Type 2 n = 93, Type 1 n = 1.
Ungradeable images	Photos were graded in 5 grades, 5 being the best quality. The average grades assigned by the three doctors were 3.8 ± 0.6 for the 3x3 and 4.0 ± 0.7 for the 9 field collage without mydriasis. The average grades assigned by the three doctors were 4.4 ± 0.4 for the 3x3 and 4.2 ± 0.6 for the 9 field collage with mydriasis. A significantly better evaluation was made in the quality of the fundus photographs with mydriasis than those without mydriasis both in the 3x3 ($p < 0.0001$) and the collage form ($p < 0.0001$).
Comments	In a separate adolescent study 9-field non-mydriatic images derived from 61 adolescent diabetics attending a summer camp were sent to Ophthalmologists over an analog phone line.

1.2.5.5 Studies of Optometrist's slit-lamp biomicroscopy.

In order to compare studies of optometrist's slit-lamp biomicroscopy as a method of screening they have been tabulated below into similar categories and they have been further divided into those that have compared optometrist's slit-lamp biomicroscopy with a recognised reference standard of seven-field stereo photography, an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography, and those that have not.

The best designed study described below is that of Olson[158] and Sharp[15], in which all those patients seen by an Optometrist are also examined by a retinal specialist and there is a comparison with digital photography.

In this study, slit-lamp examination by Optometrists, for the detection of sight-threatening retinopathy, achieved a sensitivity of 73% (52-88) and a specificity of 90% (87-93). No technical failure was reported. Using two-field imaging, manual grading of red-free digital images achieved a sensitivity of 93% (82-98) and a specificity of 87% (84-90). The technical failure rate for digital imaging reported was 4.4% of patients.

Photographic methods of screening achieve higher sensitivities and specificities for screening than slit-lamp biomicroscopy by a number of trained Optometrists.

Studies assessing Optometrist's slit-lamp biomicroscopy with a reference standard of seven-field stereo photography or an Ophthalmologist using slit-lamp biomicroscopy or fluorescein angiography:

Year	Author	Number of patients in study (n) patients (p) eyes (e)
1996	Hammond[202]	n = 474 e.
	Methods	Slit lamp biomicroscopy examination by a single ophthalmic optician, using a 78D lens.
	Reference standard	Slit lamp biomicroscopy by an experienced clinical assistant in ophthalmology, using a 78D lens.
	Outcome measure	Presence of any DR, presence of moderate or severe background, presence of moderate to severe maculopathy.

	Result	There was total agreement about presence or absence of retinopathy in 366 eyes (77%). Although the optician diagnosed less background diabetic retinopathy (83 versus 123 eyes) and diabetic maculopathy (47 eyes versus 63 eyes), he would have referred 20 of 26 eyes with moderate or severe maculopathy and 33 of 36 eyes with moderate or severe background retinopathy: sensitivities of 0.77 and 0.92 respectively (no confidence intervals given). Specificity 1.0 because the Optometrist did not refer any patient that the Ophthalmologist did not.
1998	Burnett[203]	n = 90 (of 536 screened).
	Methods	Slit-lamp biomicroscopy by 63 locally accredited Optometrists.
	Reference standard	n = 90p, 45 from the screen negative group and 45 from the hospital diabetic clinic and review of hospital records of all cases referred for an opinion about DR over 6 months.
	Outcome measure	Detection of referable DR.
	Result	Sensitivity 100%, specificity 94% (CI 90-98).
2001	Prasad[204]	n = 429 (9.67%) re-examined of 4438 screen negative reports. n = 371 screen positive patients.
	Methods	Slit-lamp biomicroscopy by 27 locally accredited Optometrists.
	Outcome measure	Detection of sight threatening diabetic retinopathy (STDR).
	Result	The sensitivity for identification of STDR was 76% (95% CI 70% to 81%) and specificity 95% (95% CI 95% to 96%). The technical failure rate was 0.2%.
2002	Hulme[205]	n = 439 of 878 invited for rescreening from 3186 screened.

	Methods	Trained Optometrists using slit-lamp biomicroscopy and Volk lenses (78 dioptre).
	Reference standard	Ophthalmologist performing slit-lamp bio-microscopy.
	Outcome measure	Detection of any retinopathy and of sight threatening eye disease (STED).
	Result	Sensitivity for any retinopathy was 72%, specificity 77%. For STED, in this group, sensitivity was 87% and specificity 91%. No confidence intervals were given.
2003	Olson[158] and Sharp[15]	n = 586 p.
	Methods	Slit-lamp biomicroscopy performed by trained Optometrists.
	Reference standard	Slit-lamp biomicrocopy by retinal specialists.
	Outcome measure	Any retinopathy, clinically significant macular oedema and sight-threatening retinopathy (otherwise described as referable).
	Result	For the detection of any retinopathy, Optometrists examination - sensitivity of 75% (CI 67-83) and specificity of 82% (79-86). For the detection of clinically significant macular oedema, Optometrists examination - sensitivity of 46% ((19-75) and specificity of 92% (90-95). For the detection of sight-threatening retinopathy (referable), Optometrists examination - sensitivity of 73% (52-88) and a specificity of 90% (87-93).
2004	Tu[206]	n = 113 screen negative patients examined, 109 screen positive patients examined (of 1643 patients screened).
	Methods	Comparison of slit-lamp biomicroscopy performed by Optometrists with a total number of screens of 769 per annum and hospital based digital photographic screening service with a total number of screens of 874 per annum.

Reference standard	An Ophthalmologist's slit-lamp biomicroscopy of 55 patients referred with ?cataract/glaucoma and the Optometrist found no DR and 68 screen negative patients audited from the digital photography model.
Outcome measure	Referable retinopathy.
Result	Sensitivity for optometry model of 75%, and specificity 98%. Sensitivity for optometry model for digital photography of 80% and specificity of 98%.

1.2.5.6 Studies assessing an Ophthalmologist's slit-lamp biomicroscopy as a reference standard.

Examinations by retinal specialists using contact-lens biomicroscopy (CLBM) compared favourably with 7-field stereo photography for the detection of macular oedema in the ETDRS study reported by Kinyoun[207]. Some studies that have reported the detection of any DR detected by an Ophthalmologist's slit lamp biomicroscopy with a 90D, 78D or 60D lens (Kalm[155], Lee[160], Schachat[161]) have shown good results with some under reporting. Some studies that have reported sight-threatening levels of DR detected by an Ophthalmologist's slit lamp biomicroscopy with a 90D, 78D or 60D lens (Kalm[155]and Lee[160]) have shown good results with some under reporting.

In the study by Pugh[138], in which Ophthalmologists in one of the two centres used slit-lamp biomicroscopy, very poor results were obtained. However, the number of subjects that had an examination that included slit-lamp biomicroscopy was not stated, nor whether this affected the examination results. In the study by Lin[183], nine Ophthalmologists (all board-certified) performed very poorly using slit-lamp biomicroscopy in determining the threshold used in the study for referral to further ophthalmological evaluation (ETDRS level ≥ 35).

The results of the studies summarised below suggest that although an Ophthalmologist's examination can perform well as a reference standard, it cannot be assumed that an individual Ophthalmologist will perform well. Retinal specialists have performed better than general Ophthalmologists in the above studies.

Hence the Gloucestershire Diabetic Eye Study includes a validation study (study 1) of the Ophthalmologist's slit lamp biomicroscopy versus seven field stereo-photography, the former being the reference standard for study 2.

Year	Author	Number of patients in study (n) patients (p) eyes (e)
1989	Kalm[155]	n = 185 p with type II diabetes.
	Methods	Two 45 degree non-stereo 35mm mydriatic fundus photography and indirect slit lamp biomicroscopy using a 60D lens by one Ophthalmologist.
	Reference standard	Estimation of the true prevalence taken from these two methods.

	Outcome measure	Detection of background DR, pre-proliferative DR, proliferative DR and diabetic maculopathy.
	Result	The sensitivity of the photographic method was 87/97% (right eye/left eye) when detecting background retinopathy and 81/80% for maculopathy versus 69/61% and 79/63%, respectively, with the slit-lamp method.
1989	Kinyoun[207]	n = 1868 p from the ETDRS study.
	Methods	7 field stereo-photography.
	Reference standard	Mydriatic slit-lamp biomicroscopy with a fundus contact lens (CLBM) by retinal specialists in 22 clinical centres.
	Outcome measure	Diabetic macular oedema.
	Result	Based on clinical detection, 53% (1778 patients) had hard exudates within 1 disc diameter (DD) of the centre of macula, 56% (1868 patients) had retinal thickening within this region, and 31% (1027 patients) had thickening at the centre of macula. These analyses show agreements of 83%, 78%, and 83% between retinal specialists and photographic graders when assessing these three characteristics, respectively. Agreement was 81% in the detection of macular oedema for which treatment is indicated (clinically significant macular oedema).
1993	Pugh[138]	n = 352.
	Methods	An Ophthalmologist's examination through dilated pupils using direct and indirect ophthalmoscopy. Two centres were used, 10 Ophthalmologists performed the examinations and one of the two centres used slit-lamp biomicroscopy using a 90 Dioptre lens. The number of subjects that had an examination that included slit-lamp biomicroscopy was not stated, nor whether this affected the examination results.
	Reference standard	7 field stereo-photography.

	Outcome measure	Retinopathy levels were dichotomised into none and mild non-proliferative versus moderate to severe non-proliferative and proliferative.
	Result	Overall the examination results were poor with sensitivity of 0.33, specificity of 0.99, positive and negative likelihood ratios of 72 and 0.67. Of a total of seven cases of proliferative retinopathy, the Ophthalmologist's examination only detected three.
1993	Lee[160]	n = 410 Oklahoma Indians (795 e) with NIDDM.
	Methods	One 45 degree field non-mydriatic fundus photography through dilated pupils.
	Reference standard	Binocular indirect ophthalmoscopy and slit lamp biomicroscopy with a 90 D lens by one of three Ophthalmologists.
	Outcome measure	Diagnosis of no retinopathy, non-PDR and PDR.
	Result	Of the 730 eyes that were gradeable by both methods overall agreement between the two methods in diagnosing no retinopathy, non-PDR and PDR was 86.3% with a kappa statistic kappa of 0.74 was found. For the diagnosis of proliferative diabetic retinopathy (PDR), there was an agreement of 98.1% with a kappa of 0.84. With a total of 61 cases of proliferative retinopathy diagnosed by either method in our study, ophthalmoscopy alone detected 88.5% and fundus photography, 78.7%. In the five eyes that were diagnosed by fundus photography and not by the ophthalmological examination all 5 eyes had non-PDR diagnosed and none satisfied the high-risk criteria.
1993	Schachat[161]	n = 1168 p (history of diabetes in 21%).
	Methods	Two mydriatic 30 degree stereoscopic photographs of the disc and macula.

	Reference standard	Direct ophthalmoscopy and slit lamp biomicroscopy using a 78 dioptre lens, three mirror lens or both by an experienced Ophthalmologist.
	Outcome measure	Detection of any DR.
	Result	The frequency of diabetic retinopathy was 7.7% (90/1168) by clinical examination, 8.7% (102/1168) by photographic grading, and 6.7% (78/1168) by both methods.
2002	Lin[183]	n = 197 p.
	Methods	Single 45 degree field digital monochromatic non-mydriatic photography and dilated binocular indirect ophthalmoscopy and slit-lamp biomicroscopy by nine Ophthalmologists (all board-certified).
	Reference standard	7 field stereo-photography.
	Outcome measure	Threshold for referral to further ophthalmological evaluation (ETDRS level $\geq$ 35).
	Result	Sensitivity of ophthalmoscopy compared with 7 field stereo-photography was 34%, with a specificity of 100%.

1.2.5.7 Studies referring to Visual Acuity as a screening method.

Visual Acuity is widely supported as an adjunct to screening for diabetic maculopathy but there is very little literature available on the subject. The only study reported in the literature is that by Corcoran in 1985, which is summarised below, and leaves many questions unanswered (such as the other causes of VA < 6/12). One of the aims of the Gloucestershire Diabetic Eye study was to assess the value of Visual acuity measurement in Diabetic Retinopathy Screening.

Studies referring to Visual Acuity in screening for diabetic maculopathy:

Year	Author	Number of patients in study (n) patients (p) eyes (e)
1985	Corcoran[208]	N = 197.
	Methods	The best correct visual acuity (VA) was recorded under standardised conditions in 197 of 223 randomly selected patients > 50 years old.
	Reference standard	'Examination by an Ophthalmologist'. One assumes that this was direct ophthalmoscopy.
	Outcome measure	Best corrected VA < 6/12.
	Result	True VA was < 6/12 in one, or both eyes, of 69 patients (35%). Twenty-two per cent of patients with subnormal acuity had diabetic maculopathy compared with 1% of those with normal acuity.

1.2.5.8 Studies of other methods of screening for diabetic retinopathy.

Two new techniques have recently shown promise. Neubauer[209] reported encouraging results in 31 eyes using a Retinal thickness analyser (RTA) combined with a red free fundus photograph in the detection of macular oedema and PDR. Ong[210] reported encouraging results in 510 eyes using the automated tritan contrast threshold (TCT) for the detection of sight threatening diabetic retinopathy (STDR). Eyes with a best corrected Snellen visual acuity (BCVA) of worse than 6/9 were one of the exclusions in this study.

Both these methods show potential but further work is needed before they are widely adopted.

1.2.5.9 Numbers and types of fields for photographic screening.

The optimum number of fields for screening for sight threatening diabetic retinopathy is not clear at the present time, as the evidence is controversial. The outcome measure for the studies in the literature is variable.

Moss[211] compared retinopathy levels derived from the detailed grading of all seven standard 30 degree photographic fields of 2694 diabetic persons with those derived from combinations of two, three or four fields. For eight retinopathy levels, the rate of agreement with seven fields ranges from 80% for two fields to 91% for four fields.

Aldington[212] compared grading of 2 x 45 degree 35mm retinal photography with 7-field stereo-photography but there were only 48 eyes in this study.
Olson[158] & Sharp[15] compared one and two 50 degree field mydriatic red free digital photography in 586 patients and found very similar sensitivities and specificities. Manual grading of two-field red-free digital images gave a sensitivity of 93% (82-98) and specificity of 87% (84-90). Single macular field only sensitivity of 93% (CI 83-98) and specificity of 87% (CI 84-90).
Two studies by Von Wendt[213 214] recommended two 60 degree field mydriatic photographs. In the second study the results showed that testing of one macular centred 45 degree field disclosed 73% of NVE's detected in one 60 degrees fovea-centred photograph and 53% of those detected in two. Two-field 45 degrees photography disclosed 77% of NVE's detected by two-field 60 degrees photography.
The results from Moss[211] and Von Wendt[213 214] suggest that a larger area of retina that is photographed will have a higher level of retinopathy detection and the study by Olson[158] & Sharp[15] suggests that there is no additional benefit in a nasal field being added to a singular macular field.
Bresnick[215] retrospectively analysed of data from 3711 patients with diabetes enrolled in the Early Treatment Diabetic Retinopathy Study (ETDRS). He found that haemorrhages and microaneurysms (h/ma) temporal to the macula (photographic field 3), as severe as or more severe than ETDRS standard photograph 1 (h/ma 3 > or = 3), identified 87% to 89% of eyes with PDR and 92% to 93% of eyes with moderately severe to severe NPDR, which are at high risk for developing PDR. Any hard exudates within one disc diameter of the macular centre detect CSME with sensitivity 94%, specificity 54%. This suggests that CSME can be successfully diagnosed by the presence of hard exudates < 1DD from the foveal centre.

The Gloucestershire Diabetic Eye study used two 45 degree fields for the mydriatic digital photography (EURODIAB protocol) and one 45 degree field for the non-mydriatic photography. The reason for including only one field for non-mydriatic photography was that it was considered that it might be difficult for the screeners to capture a nasal field without mydriasis.

1.2.5.10 Compression Studies.

Three previous studies have looked at the maximum acceptable level of JPEG compression of digital images of diabetic retinopathy.

In the Eikelboom[216] study, only 15 eyes were included. In the Newsom[217] study, forty-seven 35 mm slide photographs were scanned at a resolution of 3000 dots per inch (dpi) into TIFF files with a size of 4.68Mbytes. They were then subjected to different levels of JPEG compression. The corresponding sensitivities for retinopathy grading and specificities were measured. They demonstrated a significant loss of sensitivity of retinopathy grading with increasing levels of JPEG compression compared with the original slide film. The best evidence available comes from a recent study by Basu[218]. The study used a Sony DXC 950 P 3CCD colour video camera mounted on a Canon CR6 45NM*f* fundus camera and the original bitmap images were compressed using the JPEG algorithm within Adobe Photoshop (version 4.0). The original captured image was a size of approximately 1,270 kilobytes (smaller than many of the current generation of digital cameras). The study concluded that only some degree of image compression (compression ratios of 1:20 to 1:12) with file sizes of 66 – 107 kilobytes is permissible using JPEG format, whereas the images obtained after higher compression ratios may not be suitable for diabetic retinopathy screening.

There are two elements of concern for the English Screening Programme:

a) There is a realisation that modern digital cameras do often compress within the camera at capture.
b) With modern digital cameras the original image may be very large and compression may be necessary for easy viewing from a server when a patient is seen in clinic.

Hence the following guidance has been given for the English screening programme:

1. The Camera Specification Document prepared by the Four Nations Working Group (available on the website www.nscretinopathy.org.uk) recommended that image file storage formats should not result in the loss of any clinically significant information. The reason for this was that there was a realisation that modern digital cameras do

sometimes compress within the camera at capture. At the point of capture the original digital images can vary in size between 1 megabyte and 20 megabytes. Compression algorithms within many of these camera backs are a closely guarded secret, but lower levels of compression in these cameras do not appear to result in the loss of any clinically significant information. Current evidence is limited but, based on the information we have, a reasonable guide would be to restrict JPEG compression to a maximum of 20:1. It would be sensible to use the highest quality JPEG compression setting on current cameras.

2. Second compressions are more likely to result in the loss of clinically significant information, and schemes undertaking second compressions should carefully test these systems.
3. It is recommended that grading is always in the original captured format. Once captured, this is the format that should be graded before any compression or further compression is undertaken to this image. This original image will need to be kept for 8 years, even after grading, so that reference can be made to this original image in the future if required.

1.2.5.11 Reviews and reports on screening for diabetic retinopathy.

In 1989, a qualitatative assessment by Rohan[219] concluded that screening and early treatment of retinopathy would prevent deterioration of visual acuity and could reduce the risk of blindness due to diabetic retinopathy by an estimated 56% and prevent 260 new cases of blindness in diabetics under the age of 70 each year in England and Wales. Further support for screening for retinopathy was provided by the Retinopathy Working Party[220] who were participants in a Workshop for the Definition of a Protocol to Screen for Diabetic Eye Disease in Europe in London in 1990 and by a review by Singer[3]. MacCuish[2] pointed out that none of the available options will ensure eye screening for young defaulters with insulin-dependent diabetes, estrange or alienated from all medical care, whose only regular contact is for renewal of insulin prescriptions. Evidence for this being a high-risk group was supported by a retrospective audit of medical records by Jones[221].

In 1995, Ryder[142] recommended screening using the combined modality of dilated retinal photography and direct ophthalmoscopy. In the same year, the St Vincent Joint Task Force[222], which was established in 1992, jointly by the Department of Health (DH)

and the British Diabetic Association (BDA) to advise on the implementation of the 'St Vincent Declaration' reported four priority needs of the Visual Impairment Subgroup, the first of which was a formally structured retinopathy screening programme.

1996, Bachmann & Nelson[5] produced a report entitled 'Screening for diabetic retinopathy: A quantitative overview of the evidence, applied to the populations of health authorities and boards'. In this report it stated that, for a total population of half million, about 5000 would have diabetes. If all of these were screened, about 4% would be detected as requiring treatment during an initial screening round, but this yield would decreased to about 2% in subsequent annual screening rounds. Of those treated, the population prevented from going blind would be 6% within a year of treatment and 34% within ten years of treatment. Bachmann later published an evidence-based model[223] recommending screening for diabetic retinopathy.

In 1996, the Scottish Health Purchasing Information Centre (SHPIC) produced a report[4], which concluded that digital cameras are a promising new technology, with a number of advantages over current cameras. However, digital screening needs to be evaluated through a proper trial in field conditions. Until this research is done, it is not recommended for routine use.

In 1997, Backlund[224] reported that new blindness in diabetes had reduced by more than one-third in Stockholm county following the introduction of a community-wide mobile fundus photographic screening programme using 35mm film. In the same year the British Diabetic Association produced two reports[225 226] outlining the considerations involved in setting up a screening service based 1) upon retinal photography or 2) slit-lamp biomicroscopy by Optometrists.

In 1997 the Royal College of Ophthalmologists produced a report[227] entitled 'Guidelines for Diabetic Retinopathy'. This report recommended a) all patients over 12 years and/or entering puberty should be screened b) screening should be performed annually and c) screening should be performed in the most appropriate and comprehensive manner.

In 1999, the NHS Centre for Reviews at the University of York produced a bulletin[228] and journal publication[229] recommending that screening can be effectively provided by trained and accredited Optometrists or by retinal photographers in a variety of locations.

In 2000, a review by Hutchinson[6] concluded that, based on an assessment of available cohort studies, the most effective strategy for testing is the use of mydriatic retinal

photography with the additional use of ophthalmoscopy for cases where photographs are ungradeable.

In 2000, Garvican[7] and Gillow[9] reviewed the findings of a group commissioned by the National Screening Committee to develop a model for a comprehensive national risk-reduction programme in the UK. The group proposed the introduction of a systematic national programme based on digital photography.

In 2000, Pandit[230] reviewed published data from 1933-1999 and concluded that the risk of inducing acute glaucoma following mydriasis with tropicamide alone is close to zero, no case being identified.

In 2001, a report[11] by the Scottish Intercollegiate Guidelines Network (SIGN) recommended that systematic annual screening for diabetic retinal disease should be provided for all people with diabetes.

In 2002, a report[12] by the Health Technology Board for Scotland (HTBS) recommended that a national diabetic retinopathy screening programme for Scotland should be established to detect referable (sight-threatening) retinopathy using a three-stage process based on non-mydriatic digital cameras, with the use of mydriasis and slit-lamps, where necessary.

The National Institute for Clinical Excellence in it's draft report[10] in 2000 and final guideline in 2002 entitled 'Retinopathy – screening and early management' recommended that the eyes of people with type 2 diabetes are screened at the time of diagnosis and at least annually thereafter. Screening should use tests with a sensitivity $\geq 80\%$, specificity $\geq 95\%$ and technical failure rate $\leq 5\%$.

In 2002, a report[14] entitled the 'National Service Framework for Diabetes: Delivery Strategy' announced the introduction of a National Screening Programme for Sight-Threatening Diabetic Retinopathy in England. The target given by the NSF was that "by 2006, a minimum of 80% of people with diabetes to be offered screening for the early detection (and treatment if needed) of diabetic retinopathy as part of a systematic programme that meets national standards, rising to 100% coverage of those at risk of retinopathy by end of 2007".

In 2002, Younis[231] reviewed the current status of retinopathy screening schemes in the UK and found that many health authorities have ad hoc screening programmes reaching only about 60% of patients, with unacceptable or undocumented efficacy and minimal quality control. This article received further correspondence from Morris[232] et al pointing out that that, the developments in Scotland.

In 2003, Harding et al[233] recommended a single grading structure to be used for screening programmes in England and Wales although, in the same year, Wilkinson et al[234] proposed an international clinical diabetic retinopathy and diabetic macular oedema disease severity scales, which was more suited to the American Medical system.

In 2003, the National Institute for Clinical Excellence draft report[16] entitled 'Type 1 diabetes: management of Type 1 diabetes in adults in primary and secondary care' recommended that eye surveillance for newly diagnosed with Type 1 diabetes post-puberty should be commenced from diagnosis using mydriatic digital photography.

In 2004, a survey[235] in England and Wales of coverage in screening for diabetic retinopathy by Wilson found that, of twenty-five health authorities in England and Wales sampled, nine did not have a population-based screening scheme, six had an optometry scheme, six had a camera scheme and four had schemes with more than one method of screening ('mixed schemes').

In conclusion, reviews and reports have increasingly recommended screening for diabetic eye disease and the majority have recommended photographic screening. There is, however, a lack of studies evaluating mydriatic and non-mydriatic digital photography in a screening environment. The Gloucestershire Diabetic Eye study was designed to test both mydriatic and non-mydriatic digital photography in a screening environment.

1.2.6 Are the costs of screening and effective treatment of sight-threatening diabetic retinopathy balanced economically in relation to total expenditure on health care - including the consequences of leaving the disease untreated?

In 1982, Savolainen[236] reported on the cost-effectiveness of photocoagulation for sight-threatening diabetic retinopathy in the UK. There have been reports of computer simulation models by Javitt[237 238 239 240], Dasbach[241], Caro[242] and Fendrick[243] but these were based on the health systems in the USA and Sweden[244] and hence need to be interpreted with caution in the UK. Modelling studies from the Wessex Institute[245] suggested that there is greater benefit in reducing the screening interval when the screening programme retains patients until they require treatment than when the screening programme detects early, background retinopathy, with prompt referral to specialist services.

Bachmann and Nelson[5] summarised the economic literature on screening for diabetic retinopathy prior to 1996. They found that British cost and cost-effectiveness analyses suggest that screening by retinal photography or optician may be at least as efficient as retinal examination by general practitioners or Ophthalmologists, although one study[246] [247] showed examination by clinical assistants in ophthalmology to be most cost effective. They commented that a recent British report[248] estimated the direct health service cost of screening by retinal photography to be £13 per screening episode. James et al[249] reported results for an organised screening programme using 35mm retinal photography and demonstrated this to be more cost-effective than the previous system of opportunistic screening.

Meads[250] reviewed published studies of the costs of blindness and compared Fould's 1983 estimate[25] inflated to £7,433 in 2002 costs, Dasbach's 1991 estimate[241] inflated to £5391 in 2002 costs and Wright's 2000 estimate[251] inflated to £7452 (4,070 - £11,250) in 2002 costs. He concluded that much of the uncertainty in any sensitivity analysis of the cost of blindness in older people is associated with the cost of residential care and that the excess admission to care homes caused by poor vision is impossible to quantify at the present time.

Only two studies have assessed the costs of screening using digital photography. Bjorvig[252] assessed the costs of telemedicine screening for diabetic retinopathy in a trial conducted in northern Norway. At low workloads, telemedicine was more expensive than conventional examination. However, at higher workloads, telemedicine was cheaper. The break-even point occurred at a patient workload of 110 per annum. Tu[206] calculated the cost of screening each patient as £ 23.99 per patient for an optometry model and £ 29.29 per patient for a digital photographic model. However, in this study there was poor compliance rates in the newly introduced screening programme in both models.

The UK National Screening Committee has recommended digital imaging as the preferred method of retinal photography for screening[8 253]. They have used estimates of costs by Garvican[253] for a theoretical population of 500,000. For a mobile photographic screening service, the cost of the initial screen is estimated as approximately £21 per diabetic patient registered or £24 per attendee at 85-90% uptake.

One aspect of the design of the Gloucestershire Diabetic Eye study was to assess the costs and cost-effectiveness of a digital photographic screening programme.

Studies of cost-effectiveness of screening for diabetic retinopathy, blindness and treatment have been tabulated below.

Relevant studies are as follows:

Year	Author	
1982	Savolainen[236]	Cost-effectiveness of photocoagulation in the UK. 1978 costs - out-patient photocoagulation treatment and follow-up comes to £60 per eye per year, or £100 per patient per year. Maintaining one blind person per year due to diabetic retinopathy (considering loss of average earnings and social security payments) comes to £1,751 per annum.
1983	Foulds[25]	Estimated the cost of blindness to be £3,575 per annum for a person in the 40's age group and the cost per annum of identifying and treating patients at risk of blindness to be £387 per patient treated.
1989	Javitt[237]	Cost effectiveness of current approaches to the control of retinopathy in type 1 diabetes.
	Computer simulation model	Model predicts a cost of $966 per person-year of vision saved from proliferative retinopathy and $1118 per person-year of central acuity saved from macular oedema. This is only one seventh of the $6900 average cost of 1 year of Social Security Disability for those disabled by vision loss in the USA.
1990	Javitt[238]	
	Computer simulation model	Screening for and treating retinopathy in patients with type I diabetes mellitus was cost-effective using all screening strategies.
1991	Dasbach[241]	Cost-effectiveness of screening and treatment for diabetic retinopathy.
	Computer simulation model	Generally costs of screening programs appear to be recovered by avoided costs of blindness in the population subgroups taking insulin; however, the cost of screening programs generally are not recovered by avoiding costs of blindness in the older onset population subgroup not taking insulin.

1991	Sculpher[246]	Cost and cost-effectiveness of different methods of screening
1992	Sculpher[247]	diabetic patients for sight-threatening retinopathy. Screened by GP - sensitivity 65%, specificity 84% - expected cost per true positive detected £650 (expected cost per screen £24). Screened by Optician - sensitivity 61%, specificity 87% - expected cost per true positive detected £631 (expected cost per screen £22). Screened by GP-visiting camera - sensitivity 68%, specificity 90% - expected cost per true positive detected £443 (expected cost per screen £18). Screened by hospital-based camera - sensitivity 55%, specificity 89% - expected cost per true positive detected £863 (expected cost per screen £27). Screened by GP + GP-visiting camera - sensitivity 85%, specificity 80% - expected cost per true positive detected £679 (expected cost per screen £33). Screened by Optician + GP-visiting camera - sensitivity 75%, specificity 83% - expected cost per true positive detected £842 (expected cost per screen £37).
1992	Fendrick[243]	To simulate the health and economic outcomes of an annual screening programme for retinal disease in a cohort of Type 1 diabetes mellitus patients in Sweden using recent study[244] data.
	Computer simulation model	Over a screening acceptance rate of 60-100%, the estimated net savings in present value figures over the 60-year period, including all of the costs of screening and treatment, range from 22 to 37 million SEK (US $3.7 to $6.0 million).
1992	Lairson[254]	Cost-effectiveness of different screening options.

		Medical system costs per true positive were: 45 degrees photos with dilation, $295; 45 degrees photos without dilation, $378; Ophthalmologist, $390; and technician, $794. Patient costs per true positive were: 45 degrees photos with dilation, $139; 45 degrees photos without dilation, $171; Ophthalmologist, $306; and technician, $1009.
1993	Torgerson[255]	Recruitment methods for screening programmes. Open letters of invitation achieved efficiency by increasing the number of women screened with given resources within a larger population.
1994	Javitt[239]	
	Computer simulation model	Demonstrated that screening and treatment for eye disease in patients with type II diabetes generates annual savings of $247.9 million to the federal budget.
1996	Bachmann & Nelson[5]	'Screening for diabetic retinopathy: A quantitative overview of the evidence, applied to the populations of health authorities and boards'.
	Summary	British cost and cost-effectiveness analyses suggest that screening by retinal photography or optician may be at least as efficient as retinal examination by general practitioners or Ophthalmologists, although one study shows examination by clinical assistants in ophthalmology to be most cost effective. The most recent and largest British report[248] estimated the direct health service cost of screening by retinal photography to be £13 per screening episode.
1996	Javitt[240]	
	Computer simulation model	Screening and treatment of eye disease for patients with insulin-dependent diabetes mellitus costs $1996 per quality-adjusted life-year (QALY) saved, those with non-insulin-dependent diabetes mellitus (NIDDM) who use insulin for glycaemic control costs $2933 per QALY, and those with NIDDM who do not use insulin for glycaemic control costs $3530 per QALY.

1998	UKPDS[256]	Estimated the economic efficiency of tight blood pressure control. Based on use of resources driven by trial protocol, the incremental cost effectiveness of tight control compared with less tight control was cost saving.
1999	Wessex Institute[245]	Health Research and Development report, which considered the proposal to reduce the interval for diabetic retinal screening from one to two years.
	Complex simulation models	The modelling studies suggest that there is greater benefit in reducing the screening interval when the screening programme retains patients until they require treatment than when the screening programme detects early, background retinopathy, with prompt referral to specialist services.
2000	Garvican[7]	Estimated: 'The cost of the screening programme will be about £1370 per case treated in the first year. This rises to £1900 per case treated in year 4, but that by then the programme could be funded out of revenue savings from the cost of symptomatic treatment'.
2000	James[249]	Cost-effectiveness analysis of screening for sight threatening diabetic eye disease using data from the Liverpool Diabetic Eye Study. The cost-effectiveness of the systematic programme was £209 (sensitivity 89%, specificity 86%, compliance 80%, annual cost £104,996) and of the opportunistic programme was £289 (combined sensitivity 63%, specificity 92%, compliance 78%, annual cost £99,981). The incremental cost effectiveness of completely replacing the opportunistic programme was £32.
2000	RNIB[257]	The Royal National Institute for the Blind report entitled 'The costs of blindness'. This report confirmed that it is very expensive to be visually impaired with significant extra costs being incurred in meeting daily living needs.
2000	Vijan[258]	Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus.

		The marginal cost-effectiveness of screening annually vs. every other year varies; patients in the high-risk group cost an additional $40530 per QALY gained, while those in the low-risk group cost an additional $211570 per QALY gained.
2000	Wright[251]	The direct costs of blindness in Australia. Case 2 was a working aged person with diabetic retinopathy. The annual cost for case 2 was $17701 ranging from $9669 to $26720. The costs include pensions, subsidies, concessions, equipment and services.
2001	Lee[259]	The costs of mobile screening for diabetic retinopathy. Costs for mobile screening were estimated to be A$41 per participant screened.
2001	Sharma[260]	The cost-effectiveness of early vitrectomy for the management of vitreous haemorrhage secondary to diabetic retinopathy.
	Markov model	The cost per additional QALY gained from early vitrectomy treatment was $1910 (US$ discounted at 3%).
2002	Bjorvig[252]	The costs of telemedicine screening for diabetic retinopathy in a trial conducted in northern Norway. A cost-minimisation analysis showed that at low workloads, for example 20 patients per annum, telemedicine was more expensive than conventional examination. However, at higher workloads, telemedicine was cheaper. The break-even point occurred at a patient workload of 110 per annum.
2002	Caro[242]	The lifetime costs associated with complications of type 2 diabetes.
	Complex simulation model	The costs of complications were estimated to be $47,240 per patient over 30 years, on average. Retinopathy accounts for 10% of the costs of complications.
2002	Davies[261]	Cost effectiveness of varying the screening method and the screening interval.

	UK model	The mobile camera, used for annual screening and 6-month follow-up after the detection of background retinopathy, had an estimated cost of £2842 per sight year saved. The authors concluded that results indicate that it appears more cost effective to continue to screen outside an ophthalmology clinic, until treatment is needed.
2002	Gandjour[262]	The UK rated as both the most effective and the most efficient country in providing secondary prevention in Type 2 diabetes.
2003	Anderson[166]	The cost of screening for diabetic eye disease in homebound nursing home residents. Total cost £16,980; cost per screen event £60.30.
2003	Clarke[263]	Using the model developed and data on 5102 UKPDS patients, the estimate of the cost of first complications was as follows: cataract extraction £1553 (£1320 - £1855); and blindness in one eye £872 (£526 - £1299).
2003	Meads[250]	The costs of blindness. The published estimates of the cost of blindness in diabetic retinopathy were equated to December 2002 rates: Fould's 1983 estimate[25] was inflated to £7,433 in 2002 costs. Dasbach's 1991 estimate[241] was inflated to £5391 in 2002 costs. Wright's 2000 estimate[251] was inflated to £7452 (4,070 - £11,250) in 2002 costs. Much of the uncertainty in any sensitivity analysis of the cost of blindness in older people is associated with the cost of residential care. The excess admission to care homes caused by poor vision is impossible to quantify at the present time.
2003	Sharp[15]	Health Technology Assessment report. Costings information was given for the study but the authors concluded that the extrapolation to a more general context of a national screening programme needs to be taken cautiously.

		For a cohort of 1000 patients screened in 1998-99, the cost per true positive detected was £420 for manual grading of digital images, £460 for automated grading of digital images, £450 for manual grading of 35mm slides and £583 for optometric screening with slit-lamp biomicroscopy.
2004	Garvican[253]	Costings information on NSC retinopathy website. Estimated costs are only, based on a theoretical population of 500,000. For a mobile photographic screening service, the cost of the initial screen is estimated as approximately £21 per diabetic patient registered or £24 per attendee at 85-90% uptake. This does not count costs of referrals and treatment, which are also detailed in the report. Once these costs have been included, the cost of the screening programme would be approximately £1490 per case treated in the first year. This rises to £2150 per case treated in year 4, but by then the programme can be largely funded out of revenue savings from the cost of symptomatic treatments. Overall the programme is therefore likely to cost about £12,000 per prevention of severe visual loss, depending on the case-mix.
2004	Tu[206]	The cost of screening each patient was calculated as £ 23.99 per patient for the optometry model and £ 29.29 per patient for the digital photographic model. The cost effectiveness was calculated as £832 for the optometry model (£18,454 / 22) vs. £853 for the digital imaging model (£25,599 / 30) in the first year. There was poor compliance rates in the newly introduced screening programme in both models.

1.2.7 Own work leading up to current study.

In 1995/6 Gloucestershire Primary Care Clinical Audit Group co-ordinated a countywide audit,[264] which identified 9556 people with diabetes over the age of 16 (2.1% of the county's population).

The results of the audit showed that 5663 (59%) of the 9556 people with diabetes (over the age of 16) in the county were under the sole care of their General Practitioner. Considerable variation was demonstrated in the arrangements for testing diabetic patients' eyes for retinopathy. Examinations had been performed by GPs, Optometrists, diabetic physicians and Ophthalmologists. There was no record of an eye examination in the previous 15 months in 25% of these and a further 7% had no record of the results of eye examinations that had taken place. In those who had been examined retinopathy was recorded in only 18% and 88% of all patients in whom retinopathy had been detected had been referred to the hospital service. This suggested that retinopathy was being missed, and that where it had been detected, unnecessary referrals were being made. This was confirmed by an audit of new referrals to the hospital eye service which showed that 20% of those referred for assessment of diabetic retinopathy had no retinopathy at all and 38% had background retinopathy with no sight-threatening features.

In response to this a mobile digital photographic screening programme was introduced in October 1998, funded by Gloucestershire Health Authority, with contributions from charitable sources.

2 Study 1.

2.1 Justification for the validation study (study 1).

There was a need to evaluate the introduction of the organised screening programme in Gloucestershire. For the design of this evaluation study (study 2), it was considered that the only possible recognised reference standard against which the screening methodologies could be tested was an Ophthalmologist's slit lamp biomicroscopy. It was not considered feasible to take a large hospital based fundus camera on the required number of visits to numerous GP surgeries in Gloucestershire with an ophthalmic photographer to perform 7-field stereo-photography.

Although an Ophthalmologist's examination can perform well as a reference standard, it cannot be assumed that an individual Ophthalmologist will perform well. Study 1 was designed to validate the reference standard of the Ophthalmologist who performed the examinations in study 1 and study 2. A further reason for the validation study was to test the two 45 degree fields recommended by Aldington[212] for the EURODIAB study against two reference standards.

2.2 Aims and objectives.

2.2.1 Aim of the validation study (study 1).

- to validate the reference standard of an experienced Ophthalmologist's examination (PS) including slit-lamp biomicroscopy by comparison with seven field stereo photography in a preselected group of patients
- to evaluate two 45 degree fields recommended for the EURODIAB study[212] using digital imaging photography against two reference standards (7-field stereo-photography and an Ophthalmologist's examination using slit-lamp biomicroscopy)
- to compare the Gloucestershire grading form with the Modified Airlie House grading used in the ETDRS study[265].

2.3. Study Design and Methods for study 1.

2.3.1 *Design and methods for the validation study (study 1).*

2.3.2 *Selection of subjects.*

A two-centre prospective evaluation study of 239 diabetic patients was carried out between December 2000 and July 2001. Diabetic subjects were recruited from the Oxford Eye Hospital diabetic retinopathy clinic, or the Bertram Diabetes Centre diabetic and eye clinic in Norwich. A research assistant on both sites identified approximately 100 suitable patients who gave a history of referable diabetic retinopathy. Controls were taken from routine patients attending the diabetic clinic in Norwich and from patients attending the eye clinic in Oxford known to have mild diabetic retinopathy or attending for conditions other than diabetic retinopathy (e.g. glaucoma). Patients with advanced cataract, on whom the ophthalmologist or diabetologist felt that it might be difficult to perform seven-field photography were excluded. A patient information sheet was posted to all patients one week prior to, and informed consent was obtained at the time of their booked outpatient appointment. Ethics committee approval was obtained from the Oxford and Norwich ethics committees.

2.3.3 *Design.*

The study was designed with 250 patients, including 100 patients with referable retinopathy, in order to have a standard error of 4% in the estimate of sensitivity. 150 patient controls were chosen in order to prevent bias in the Ophthalmologist's examination result and in the photographic grading of the seven field photographs. The Ophthalmologist and the retinopathy grading centre did not know the percentage of referable retinopathy in the study population but RM, who graded the two field digital images, was aware of this percentage. The main purpose of study 1 was to validate the ophthalmologists reference standard examination of slit-lamp biomicroscopy against seven field stereo-photography. The research registrar (RM) was tasked with the job of working out the percentage of patients with referable diabetic retinopathy so that PS was unaware and his examination would be unaffected. RM graded the two-field digital images in the study and the fact that he knew the percentage of referable DR in the study may have introduced a degree of bias into the grading of the two-field digital images.

2.3.4 *The screening process.*

All persons with diabetes attending the above clinics were considered eligible for inclusion except if they were pregnant, under 18 years of age, known to have learning or significant physical disabilities, or unwell. On arrival, visual acuity was tested using a Snellen chart at 6 metres prior to dilating both pupils using 1 drop of g. tropicamide 1% and g. phenylephrine 2.5%, repeated not more than 3 times. In the Norwich clinic phenylephrine 2.5% was restricted to patients with blood pressure less than 180/90 and only given once. Patients were then reviewed and examined in the clinic by their ophthalmic or diabetological team as part of their booked outpatient visit. This was followed by an ophthalmic examination by indirect slit lamp biomicroscopy using a 78D lens and direct ophthalmoscopy, performed by an experienced Ophthalmologist (PS). Patients then underwent 2-field mydriatic digital photography using a 45 degree Canon CR5 retinal camera in Oxford and Canon CR6 camera in Norwich. Both cameras had a Sony 3-chip video camera capturing an image of 768 x 568 pixel resolution at 24-bits colour depth. Patients then underwent 7-standard field stereoscopic 35mm slide photography using a Zeiss 30-degree retinal camera in Oxford and a Topcon 50X 35-degree retinal camera in Norwich. The examiner (PS) was masked regarding each subject's history of diabetes mellitus, and findings of current, or previous ophthalmoscopic examinations.

2.3.5 *Grading.*

All 3 methods of examination were graded independently. The ophthalmoscopic assessments were completed at the time of examination by PS, the 2-field digital images by RM and the 7-field stereoscopic 35mm slide photographs by the Retinopathy Grading Centre, London. The examiner (PS) was masked regarding each subject's history of diabetes mellitus, and findings of current, or previous ophthalmoscopic examinations although did, on occasion, have access to the patient's current visual acuity measurement. The digital and film graders were masked regarding each subject's history of diabetes mellitus, and findings of current or previous ophthalmoscopic examinations. The first two methods were graded using the Gloucestershire grading form to define referable diabetic retinopathy (Appendix 1), and the 7-field photographs were graded according to the Modified Airlie House final classification[266]. A comparison table was developed for analysis (appendix 5), by a process of matching lesions based on lesion level and severity. Referable DR was

defined as maculopathy, moderate to severe non-proliferative, proliferative and advanced retinopathy as defined by categories 3 to 6 on the Gloucestershire grading form and/or categories D to G in the comparison table. Image quality for the two field digital was determined using the criteria shown in Appendix 6. The evaluation of the quality of the seven field images was performed to determine gradeability based on strict definitions of field definition, focus/clarity and stereoscopic effect as outlined in the Early Treatment Diabetic Retinopathy Study[72] (ETDRS) Manual of Procedures. Seven-field sets, including those defined as 'ungradeable' were re-graded to include the presence of haemorrhage or exudates less than 1 disc diameter from the foveola and any proliferative or advanced retinopathy, identified in the available images. This was carried out to provide comparative data with the Gloucestershire grading procedures for these features.

Where there were discrepant results between the seven-fields stereo-photography grading by HL and the slit-lamp biomicroscopy examination by PS, they discussed the seven-field stereo-photographs and the paper results of the clinical examination. Agreement was generally reached between HL and PS from the seven-field stereo photographs as to the result that was most likely to be correct. Stephen Aldington (Manager of the Retinopathy Grading Centre) acted as a third and arbitration opinion when required. This was only needed infrequently as re-examination of the photographs usually made the result obvious.

2.3.6 *Statistical methods.*

Data were entered onto an Excel file and downloaded into SPSS* version 10 (statistics package) for data analysis as required.

Sensitivity, specificity, together with their 95% confidence intervals, and kappa values were calculated for the following comparisons:

- 2-field digital photography compared with seven-field stereo photography.
- 2-field digital photography compared with the Ophthalmologist's examination.
- The Ophthalmologist's examination compared with seven-field stereo photography.

Calculations were based on assessable images from the appropriate reference standard method. Unassessable images were then included in the sensitivity calculations when comparing other methods with the reference standard used.

The kappa values only reflect the difference between grading of referable and non-referable and not gradeable or ungradeable. It is acknowledged that the value of kappa is affected by the percentage of referable retinopathy in the population tested. By increasing the prevalence from 20 to 40%, the kappa value for measure of agreement would be increased from approximately 0.6 to 0.7 whereas the sensitivity and specificity would remain unchanged. It is therefore important not to over-interpret the kappa values obtained from study 1.

2.4 Results for the validation study (study 1).

2.4.1 *Technical failure rate and image quality.*

Ophthalmoscopic examination was technically possible in all patients. Determination of retinal status was not possible in 6 eyes of 3 patients (1.3%) from the 2-field mydriatic digital images. A total of 151 eyes (31.6%) of 7-field stereo photosets were technically unassessable using the strict quality criteria, hence were not suitable for assignment of ETDRS retinopathy level. However, when the criteria were supplemented by the additional assessment of lesions lying within one disc diameter of the foveola or presence of proliferative retinopathy, the technical failure rate reduced to 73 eyes (15.3%). All of the 6 eyes that were unassessable on two-field digital photography had assessable 7-field stereo photography using the above criteria. 5 out of the 6 eyes showed referable features both on 7-field stereo photography and the Ophthalmologist's examination.

The reasons that 73 eyes were unassessable when grading the seven field stereo-photographs was:

13 eyes - fields 1 and/or 2 were of insufficient quality for assessment

50 eyes - fields 3-7 were of insufficient quality for assessment

5 eyes - fields 1 or 2 and fields 3-7 were of insufficient quality for assessment

4 eyes - images were too dark for assessment

1 eye - images were absent.

2.4.2 *Detection of referable diabetic retinopathy.*

2.4.2.1 *Comparison of the two reference standard methods, an Ophthalmologist's examination against 7-field stereo photography.*

Comparison of the two reference standard methods, an Ophthalmologist's examination against 7-field stereo photography, in assessable eyes (Table 1) gave a sensitivity of 87.4% (confidence interval 83.5 –91.5) and a specificity of 94.9% (confidence interval 91.5-98.3). The measure of agreement was a kappa value of 0.803 (standard error 0.030).

These calculations were based on 405 eyes that had assessable seven field stereo photographs.

Table 1 - Comparison of Examination versus seven-field.

		Ophthalmologist's Examination Findings		**Total**
		No DR or non referable DR	**Referable STDR**	
Reference standard result (seven field stereo photography)	**No Dr or non referable DR**	150 94.9%	8 5.1%	158 100%
	Referable DR	31 12.6%	216 87.4%	247 100%
	Total	181 44.7%	224 55.3%	405 100%

A more detailed analysis of this result, which includes the 73 eyes that were not assessable using seven field stereo photography, is shown in Table 3.

Table 2 - Detailed comparison of Examination versus 7-field stereo photography (7-f).

	Ophthalmologist's Examination Findings							
	Not Gr	**No DR**	**Non referable DR**	**Maculopathy**	**Mod NPDR**	**Severe NPDR**	**Prolif and Adv**	**Total**
Not gradeable		29	30	6		3	5	73
(7-f)		39.7%	41.1%	8.2%		4.1%	6.8%	100%
No DR		68	2					70
(7-f)		97.1%	2.9%					100%
Non referable		35	45	4		2	2	88
DR (7-f)		39.8%	51.1%	4.5%		2.3%	2.3%	100%
Maculopathy			13	53	3	7	6	82
(7-f)			15.9%	64.6%	3.7%	8.5%	7.3%	100%
Mod NPDR			13	17	7	9	1	47
(7-f)			27.7%	36.2%	14.9%	19.1%	2.1%	100%
Severe NPDR			1	7	4	15	3	30
(7-f)			3.3%	23.3%	13.3%	50.0%	10.0%	100%
Proliferative			4	14	8	11	51	88
and advanced			4.5%	15.9%	9.1%	12.5%	58.0%	100%
(7-f)								
Total	0	132	108	101	22	47	68	478
		27.6%	22.6%	21.1%	4.6%	9.8%	14.2%	100%

2.4.2.2 *Comparison of the two-field digital photography against 7-field stereo photography.*

Comparison of the two-field digital photography against 7-field stereo photography, in assessable eyes (Table 3) gave a sensitivity of 80.2% (confidence interval 75.2-85.2%) and a specificity of 96.2% (confidence interval 93.2-99.2%). The measure of agreement was a kappa value of 0.729 (standard error 0.034).

These calculations were based on 399 eyes that were gradeable by both methods of examination.

Table 3 - Comparison of 2-field versus 7-field.

		2-field digital photography			
		No DR or non-referable DR	**Referable DR**	**Sub-Total**	**Unassessable**
Reference standard result (7-field stereo photography)	**No DR or non-referable DR**	151 96.2%	6 3.8%	157 100%	1
	Referable DR	48 19.8%	194 80.2%	242 100%	5
	Total	199 49.9%	200 50.1%	399 100%	6

2.4.2.3 *Comparison of the two-field digital photography against the Ophthalmologist's examination findings.*

Comparison of the two-field digital photography against the Ophthalmologist's examination findings, in assessable eyes (Table 4) gave a sensitivity of 82.8% (confidence interval 78.0-87.6%) and a specificity of 92.9% (confidence interval 89.6-96.2%). The measure of agreement was a kappa value of 0.758 (standard error 0.030). These calculations were based on 472 eyes that were gradable by both methods of examination.

Table 4 - Comparison of 2-field versus Examination.

		2-field digital photography			
		No DR or non-referable DR	**Referable DR**	**Sub-Total**	**Unassessable**
Reference standard result (Ophthalmologist's examination findings)	**No DR or non-referable DR**	222 92.9%	17 7.1%	239 100%	1
	Referable DR	40 17.2%	193 82.8%	233 100%	5
	Total	262 55.5%	210 44.5%	472 100%	6

2.4.2.4 *Comparison of the two reference standard methods with the Ophthalmologist's examination as the main reference standard.*

Comparison of the two reference standard methods with the Ophthalmologist's examination as the main reference standard, in assessable eyes (Table 3) gave a sensitivity of 216/224 = 96.4% (confidence interval 94.0 –98.8) and a specificity of 150/181 = 82.9% (confidence interval 77.4-88.4). The measure of agreement was a kappa value of 0.803 (standard error 0.030).

These calculations were based on 405 eyes that had assessable 7-field stereo photographs.

2.4.2.5 *Retrospective examination of the 7-field stereo photographs in which there was a difference in grading/classification between the two reference standards.*

There were eight eyes that the Ophthalmologist's examination had classified as referable retinopathy that had been graded as non-referable by seven field stereo-photography.

On looking retrospectively at the photographs of these 8 eyes:
5 eyes were classified by the Ophthalmologist as referable in whom the appropriate abnormalities were detected retrospectively on the photographs - 4 with maculopathy and 1 with referable non-proliferative retinopathy.
There were 3 patients who had abnormalities noted by the Ophthalmologist in the superior retina, 2 with new vessels and 1 with IRMA that were not detected retrospectively on the photographs, as these features lay outside the standard fields.

There were thirty one eyes that had been graded as referable retinopathy by 7-field stereo-photography and the Ophthalmologist's examination had classified as non-referable.
Of these, 12 eyes had been graded as having IRMA present on 7-field stereo photography:
Of these 12 eyes, 6 had received pan retinal photocoagulation and the IRMA had therefore been graded as present between pan retinal photocoagulation scars.
Of these 6 eyes, IRMA was retrospectively confirmed on the photographs in 5 eyes.

Of the 6 eyes that had not received pan retinal photocoagulation IRMA were retrospectively confirmed in all 6 on one of the peripheral fields (2 eyes field 6, 2 field 7, 1 field 5 and 1 field 3).

There were a further 3 eyes in whom the seven-field stereo-photographs had noted small fibrotic NVE following extensive pan retinal photocoagulation (2 in field 6 and I in field 3) that the Ophthalmologist had classified as stable treated retinopathy (i.e. non-referable). These were retrospectively confirmed from the photographs.

There were 8 eyes that had been graded as having a haemorrhage < 1DD from the foveal centre on 7-field stereo-photography. In all 8 of these eyes the Ophthalmologist had classified these as > 2 microaneurysms < 1DD from the foveal centre. Looking at the photographs retrospectively we encountered difficulties in interpretation of the ETDRS definition of haemorrhage / microaneurysm, which will be discussed below.

There were 3 eyes that had been graded as having a hard exudate < 1DD from the foveal centre on 7-field stereo photography. Retrospectively examination of the photographs confirmed that hard exudate was present in one of these eyes, a single probable drusen was present in one and no hard exudate was seen in the third, although the image quality of this third image was only just within ETDRS standard 14.

There were 2 eyes that had been graded as having a group of exudates > 1DD from the foveal centre on 7-field stereo photography. In both of these patients the Ophthalmologist had graded non-grouped exudates > 1DD from the foveal centre. Looking at the photographs retrospectively were difficulties encountered with the definition 'group of exudates' as discussed below.

There was 1 eye that had been graded as having a multiple haemorrhages on 7-field stereo photography. The Ophthalmologist had classified this eye as > 2 haems > 1DD from the foveal centre. Retrospectively it was agreed that multiple haemorrhages were present.

There was 1 eye that had been graded as having NVD present (ETDRS level 65a) on 7-field stereo-photography and classified as non-referable on the Ophthalmologist's

examination. In retrospect no NVD were visible on the photographs and this patient should have been included within the non-referable group.

2.5 Discussion relating to the validation study 1.

2.5.1 *Comparison with other studies in the literature of an Ophthalmologist's slit-lamp biomicroscopy versus 7-field stereo-photography or another photographic reference standard.*

Kalm[155] compared two 45 degree non-stereo 35mm mydriatic fundus photography and indirect slit lamp biomicroscopy using a 60D lens by one Ophthalmologist against a reference standard of estimation of the true prevalence taken from these two methods. The photographic method performed better than the Ophthalmologist with a sensitivity of 80% versus 63%, for maculopathy respectively, with the slit-lamp method. However, Kinyoun[207], described a study that was specifically designed to test for the detection of clinically significant macular oedema using 7-field stereo-photography and comparing this to mydriatic slit-lamp biomicroscopy with a fundus contact lens (CLBM) by retinal specialists in 22 clinical centres. Agreement was 81% in the detection of macular oedema for which treatment is indicated (clinically significant macular oedema).

In the study by Pugh[138], the number of subjects that had an examination that included slit-lamp biomicroscopy was not stated. Hence it is impossible to determine what effect slit-lamp biomicroscopy had on the examination results. In the study by Lee[160], slit-lamp biomicroscopy by three Ophthalmologists performed better than one 45 degree field non-mydriatic fundus photography through dilated pupils. In the five eyes that were diagnosed with PDR by fundus photography and not by the ophthalmological examination all 5 eyes had non-PDR diagnosed and none satisfied the high-risk criteria.

Schachat[161] demonstrated that the combination of direct ophthalmoscopy and slit lamp biomicroscopy using a 78 dioptre lens, three mirror lens or both by an experienced Ophthalmologist will detect most cases of diabetic retinopathy identified by disc and macula photographs read by skilled graders. However, it will lead to an underestimate of prevalence.

Only one previous study has included a complete set of patients in whom a comparison has been made between 7-field stereo photography and an Ophthalmologist's examination using slit-lamp biomicroscopy for the presence of referable diabetic retinopathy. In this study by Lin[183], nine Ophthalmologists (all board-certified) performed very poorly using slit-lamp biomicroscopy against seven-field standard stereo-photography in determining the threshold used in the study for referral to further ophthalmological evaluation (ETDRS level $\geq$ 35). In the current study, in comparison with 7-field stereo photography, the Ophthalmologist's examination gave a sensitivity of 87.4% (confidence interval 83.5–91.5%), a specificity of 94.9% (91.5-98.3%) and a kappa value of 0.803 (standard error 0.030).

2.5.2 *Reasons for differences between the Ophthalmologist and 7-field stereo-photography in this study.*

A small number of differences were explained by errors being made by both reference methods.

Definitions of referable retinopathy accounted for a significant number of differences. Particular sources of difficulty were:

a) Haemorrhage < 1DD from the central fovea was a common source of confusion with microaneurysms < 1DD often being graded instead of haemorrhage and vice versa.
b) The definition of a group of exudates > 1DD from the central foveola needs to be clearly defined.

The Ophthalmologist in this study differed from seven-field stereo-photography much more commonly in patients who had received extensive laser treatment. Although the grading form did not differentiate between IRMA in patients who had received panretinal photocoagulation and those who had not, he had not looked for IRMA in the former group. This was because he had considered the lack of new vessels to be a stable treated retina and not a referable eye. The grading form used did not allow for this difference. It perhaps illustrates the difference in performing studies to one's routine clinical practice

2.5.3 *Reasons for unassessable images in this study.*

During the clinical examination by PS, no patient was recorded as being unassessable. However patients were excluded from the study by clinic doctors if they had media opacities. These might otherwise have been technical failures for the Ophthalmologist.

A strict evaluation of the quality of the 7-field images was performed to determine assessability based on field definition, focus/clarity and stereoscopic effect as outlined in the Early Treatment Diabetic Retinopathy Study (ETDRS) Manual of Procedures (ETDRS Chapter 18). However, 7-field retinal photography in the ETDRS and similar major research trials was only carried out by extensively trained, certified and constantly monitored photographers. Even within the context of such tightly controlled retinal photography protocols it is not unusual to experience cases where the 7-field imaging fails to meet the required quality levels, with 10% technical failure rates being reported within WESDR[211]. Indeed, authors suggested in the same article that use of such a relatively complicated and difficult protocol may not be entirely necessary and fewer retinal fields may be appropriate in the context of diabetic retinopathy imaging. Technical failure rates for studies that have used a 7-field stereo protocol are not routinely reported in the literature, nor do studies report how many attempts were made to achieve an assessable seven-field set of photographs. In the study by Lin[183], 197 patients (48.5%) were excluded for unusable seven-field photos.

Within the context of the current study the patients had a much higher prevalence of retinopathy than generally amongst persons with diabetes, and consequently were more likely to have media opacities or to dilate poorly. In addition, the photographers in this study perform this technique relatively infrequently compared to the photographers in the Wisconsin studies[211], and only one chance was given to obtain a seven field set (no photographs were repeated). Hence, it proved difficult to obtain consistently high quality results in 7-field stereo imaging, with approximately 15% being technically unassessable, even when applying less strict definitions for assessability.
A review of these technically unassessable images indicated that in the majority of cases, there were sufficient images present and of sufficient photographic quality, for the presence of sight-threatening retinopathy features to have been detected, should they have been present. 7-field sets, including those defined as 'ungradeable' were therefore regraded to include the presence of haemorrhage or exudates less than 1 disc diameter

from the foveola and any proliferative or advanced retinopathy, identified in the available images. This was carried out to provide comparative data with the Gloucestershire grading procedures for these features.

2.5.4 *Performance of 2-field digital photography.*

Two-field digital photography performed well with sensitivities of >80% and specificities of >92% against both reference standards. The technical failure rate was low at 1.5%.

3 Study 2.

3.1 Justification for the main evaluation study (study 2).

The proposed method for screening for referable diabetic retinopathy in Gloucestershire was mydriatic two-field digital photography and technician direct ophthalmoscopy, which was due to commence in 1998. In1996, the Scottish Health Purchasing Information Centre[4] produced a report in which it stated that digital cameras were a promising new technology, with a number of advantages over current cameras. However, they recommended that digital screening needed to be evaluated through a proper trial in field conditions and, until this research was done, they did not recommend it for routine use. In 2002 the National Institute for Clinical Excellence produced a guideline[13] entitled 'Retinopathy – screening and early management'. In the guideline's future research recommendations it stated that 'well-designed screening studies are required to determine whether new tests of screening/early detection (such as digital camera retinal photography) meet the standards of 80% sensitivity and 95% specificity'. This topic for research has also been recommended by Lee[267] in 1999 and Younis[231] in 2002.

Non-mydriatic photography has been controversial as a method of screening. In 1991, Wareham[268] reviewed the available evidence and concluded that the current evidence was insufficient to allow it recommendation of its usage as a sole screening tool in a national screening programme for diabetic retinopathy. He concluded that there was an urgent need for properly designed studies using validated reference methods in clearly defined populations. Marks[269] came to a similar conclusion in 1992 and in 2002, the Health Technology Board for Scotland[12], despite recommending non-mydriatic photography as the first stage in their three stage screening procedure recommended the evaluation of mydriasis and multiple/single fields in screening for diabetic retinopathy In their 'topics for further evaluation'.

A combined modality of dilated retinal photography and direct ophthalmoscopy has been recommended by Ryder[142], Jacob[143], O'Hare[144],Taylor[145] and Gibbins[141]. However, it was not clear whether the advantage of adding direct ophthalmoscopy applied only to those services with screeners experienced in the technique or whether an advantage also applied with newly trained screeners. Hence the assessment of the added value of direct ophthalmoscopy was included in the design of this study.

3.2 Aims and objectives.

3.2.1 Aim of the main evaluation study (study 2).

- to measure the sensitivity and specificity of the proposed screening programme in a general practice setting compared to a reference standard
- to assess the added value of combining digital imaging retinal photography and direct ophthalmoscopy
- to compare the performance of digital imaging retinal photography with and without dilated pupils
- to consider the cost-effectiveness of the proposed screening programme.

3.3 Study Design and Methods.

3.3.1.1 *Selection of subjects.*

All patients over 16 identified as having diabetes within the general practice population studied were considered eligible for inclusion. For determination of sensitivity and specificity of the screening programme the patients acted as their own controls because they had all the investigations (including digital photographs, technician ophthalmoscopy and the gold (remove) reference standard examination) on their own eyes.

3.3.1.2 *Ethnicity.*

Ethnicity data was not collected in this study but Gloucestershire is known to have a very low prevalence of ethnic minority population of 2.8%. 97.2% of the population is white Caucasian, the largest group being from Indian origin 0.64%, black Caribbean 0.42% and mixed white/black Caribbean 0.39%.

3.3.1.3 *Type of Diabetes.*

The Type of diabetes was determined by the screener's history of the following:

Type 1 – commenced insulin within 4 months of diagnosis.

Type 2 – not requiring insulin or commenced insulin after 4 months of diagnosis.

3.3.1.4 *Justification of sample size.*

For the comparison of mydriatic photography and non-mydriatic photography in those patients with assessable images, the study was designed to detect a difference of 2% in the detection of referable DR between the methods (9% for mydriatic and 7% for non-mydriatic photography). To detect this difference with 80% power and 5% significance level, 3650 patients required to be examined, allowing for an estimated technical failure rate (unassessable image) of 15% with non-mydriatic photography. 80 groups of 50 patients from within individual General Practices were randomly selected for inclusion as potential study patients. This number allowed for lower attendance rates within some of the study practices.

3.3.1.5 *Numbers requiring the reference standard examination.*

From the Bachmann and Nelson review[5] in 1996, a sensitivity of >80% was anticipated for mydriatic photography, >60% for non-mydriatic photography and a prevalence of sight threatening diabetic retinopathy (STDR) of 10%. 1500 reference standard examinations were required to allow the sensitivity of mydriatic examination to be estimated with a 95% confidence interval of 7% either side of the point estimate (for 80% sensitivity).

Table 5 - Confidence intervals for a range of sensitivities and sample sizes.

Number requiring reference standard examination	**Sensitivity (for a true prevalence of 10% sight threatening retinopathy)**		
	60%	**70%**	**80%**
750	48-72%	60-80%	71-89%
1000	50-70%	61-79%	72-88%
1500	52-68%	62-78%	73-87%
2000	53-67%	64-76%	75-85%

3.3.1.6 *Digital photography.*

A non-mydriatic camera was used because diabetic subjects can dilate poorly and these cameras tend to be lighter and more easily transportable. At the time of commencing the study in 1998 the only camera that could offer a PC solution that was compatible with downloading the images onto the hospital Intranet was the Topcon TRC NW5s

camera with Sony 3-chip video attachment. The pixel dimensions of the original TIFF images were 768 x 576 pixels and size 1.26 MB.

3.3.1.7 *Fields taken.*

Two 45 degree fields were taken in the mydriatic group of patients (according to the EURODIAB protocol). The choice of one field for the non-mydriatic group was because of the technical difficulties in capturing a nasal field in an undilated patient.

3.3.1.8 *Grading* and *definition of 'referable sight threatening retinopathy.'*

This procedure was standardised using 19-inch monitors with settings of 1024 x 768 pixels and 32-bit colour. The software functions allowed when grading were the zoom facility, contrast/brightness and red free and not those that significantly altered the original image e.g. sharpening.

Careful attention was paid to defining what the Gloucestershire Ophthalmologists felt was an appropriate definition of 'referable sight threatening diabetic retinopathy' (referable STDR - grades 3-6 in Appendix 1) and recommendations from the European Working Party Protocol[270]. The definition reflects the stage at which it was felt that a diabetic patient should be referred into the Hospital Eye clinic.

3.3.1.9 *The reference standard.*

An Ophthalmologist's examination (PS) using 78D lens slit lamp biomicroscopy was chosen as the reference standard.

3.3.1.10 *Validation of grading and the reference standard.*

The reference standard examination of slit-lamp biomicroscopy PS was validated against seven-field stereo-photography in study 1. Study 2 was designed for RM to grade the mydriatic and non-mydriatic images of approximately 1500 patients (with a time separation between gradings) receiving the reference standard examination. It was also designed so that PS graded the mydriatic and non-mydriatic images of the remaining study patients (approximately 2,150), with a time separation between gradings (to reduce any possible memory effect). Mydriatic images from 410 research patients graded by PS were also graded by RM and by an experienced grader Helen Lipinski (HL) from the Retinopathy Grading Centre (Imperial College) to test for inter-observer variability. The eyes of these study patients were pre-selected, without the

knowledge of the graders, to include 21% that had been graded by PS at first grading as referable retinopathy. The same images were regraded by PS (after a further time separation) to test for intra-observer variability (PS1 and PS2). The study was designed in this way for comparison of grading between graders of different levels of experience in order to demonstrate that the technique is simple enough for inexperienced graders to produce good reproducible results, which would be necessary if digital photography was to be used as the preferred method for a National Screening Programme.

3.3.1.11 *Cost-effectiveness analysis.*

This was designed to compare the cost per true positive case identified by non-mydriatic digital photography alone, mydriatic digital photography alone, combined modality of mydriatic digital photography and nurse technician direct ophthalmoscopy and the previous ad hoc arrangements. Both NHS costs and costs to the patient were included. A questionnaire was designed to identify patient costs (Appendix 9).

3.3.2 Methods for the main evaluation study (study 2).

3.3.2.1 *The Gloucestershire Diabetic Eye Screening Programme.*

The screening programme was based in GP surgeries and was carried out by a nurse technician who performed two-field digital photography followed by direct ophthalmoscopy. The screener attended GP practices on pre-arranged dates. The number of days was based on the number of diabetic patients at the surgery and the forecast attendance rate. The whole of Gloucestershire (85 practices) was covered by the service and the time taken to drive to the practice varied considerably (<1 to 63 miles return to base). Greater travelling distance obviously reduced the number of patients that could be screened per day. The camera was transported on a specially designed trolley in a van with a hydroelectric lift, which enabled it to be easily moved into any general practice room that has wheelchair access. Occasionally there may be a problem finding an available room. The screener allowed 1 hour (in addition to travel time) for setting up equipment and being ready for the first patient on the first day of screening. Camera cleaning (Topcon recommendation) once a week reduced screening time by approximately 30 minutes per week. Fewer patients were seen on the final day of screening to allow time for pack up and download. Images were downloaded at least

once a week. Each day of screening took 10 to 15 minutes to download on to the network.

3.3.2.2 *Selection of subjects.*

Patients for inclusion in the study were selected by randomising groups of 50 patient (from within individual General Practices) from the numbers of diabetic patients recorded in the 1996 Gloucestershire Primary Care clinical audit. From 187 blocks of 50 patients in known practices, 80 blocks were selected at random. Five of the 85 Gloucestershire practices (with fewer than 50 diabetic patients) were not included. 3650 patients were estimated to be required for the study but additional patients were allocated in anticipation of recruitment problems in practices where attendance rates were low. 80 groups of 50 patients (4000) were allocated and the first 3650 patients screened were invited to take part. A smaller number than 3650 (3611) was required than was originally estimated to meet the requirement of a 95% confidence interval of 7% either side of the point estimate for the sensitivity result for non-mydriatic photography - remove. Reference standard patients were recruited from within this group of patients on days that the Ophthalmologist (PS) was able to attend.

3.3.2.3 *The screening process.*

The patient's details and history were taken (Appendix 2) and the patient was asked to sign the consent form (Appendix 3). Visual acuity was measured using retro-illuminated Log MAR charts (Appendix 4), modified from those used in the Early Treatment Diabetic Retinopathy Study (ETDRS)[271 272]. One 45 degree non-mydriatic digital photograph was taken of each eye using a Topcon NRW5S camera with Sony 950 video camera centred on the macula, repeated once only if necessary. The patients' pupils were then dilated with Tropicamide 1% and two 45 degree photographs, macular and nasal, were taken of each eye according to the EURODIAB protocol[162]. The screener was at liberty to take additional retinal or anterior segment views. In particular the screener was encouraged to take an anterior segment view if the images appeared blurred or if the visual acuity was lower than 6/12 and a temporal view if features of 'Moderate to Severe Non-Proliferative DR' were present (level 4 on the grading form in Appendix 1). The reason for taking anterior segment views was to assist the grader to determine the cause of partially assessable and unassessable images and the reason for the temporal views was to detect signs of proliferation in a patient at risk. Following

the photography, direct ophthalmoscopy was performed by the screener and the results were recorded. Results were graded on the basis of the two 45 degree fields first and then the additional information was considered. The graders recorded whether the additional information affected the results.

3.3.2.4 *The reference standard.*

A Haag Streit slit-lamp was transported to GP surgeries to conduct the reference standard examination. Patients for the reference standard examination were recruited from those attending for photographic screening (n=1549), on days when the Ophthalmologist (PS) was able to attend. Reference standard examinations were conducted in 34 practices across the whole of the county of Gloucestershire on 136 days over the two years, depending on room availability. Photographs and reference standard examinations were therefore performed in the GP surgeries on the same day.

3.3.2.5 *Validation of the reference standard.*

A separate study to validate the Ophthalmologist's reference standard was conducted (study 1).

3.3.2.6 *Grading and validation of grading.*

Non-mydriatic and mydriatic images were graded, using ORION* software according to the grading form (Appendix 1) with time of grading separated by at least one month to prevent bias from a memory effect. The image grading and reference standard examination both used the Gloucestershire adaptation of the European Working Party[220] guidelines for referable diabetic retinopathy, as shown in Appendix 1. Referable retinopathy was classified as grades 3 to 6 on this form. A Specialist Registrar in Ophthalmology (RM) interpreted the images from the study patients who received the reference standard examination (1549). PS (the Ophthalmologist) interpreted the images of all remaining patients who did not receive his reference standard examination (2062). Graders had a history sheet, which included details of the patient's age, diabetic and ophthalmological history, visual acuity, screener's ophthalmoscopy findings and reasons for extra views when grading study images.

It was not possible to mask the grader between methods because one image of each eye was captured without mydriasis and two images with mydriasis. For grading, 19-inch Sony Trinitron monitors were used with a screen resolution of 1024 x 768 and 32 bit

colour (although we recognise that the camera system was limited to 24 bit). The Topcon fundus camera with Sony digital camera produced an image of resolution 768 x 568 pixels.

The technical failure rate was classified as the number of patients with an unassessable image in one or both eyes, unless referable DR was detected in the other eye. Image quality was judged with reference to each eye on the macular view according to the definitions shown in Appendix 6. The nasal view was regarded as providing supplementary information and was not used for image quality assessments.

Mydriatic images from 410 research patients graded by PS were also graded by RM and by an experienced grader from the Retinopathy Grading Centre (HL) to test for inter-observer variability. The same images were regraded by PS to test for intra-observer variability.

3.3.2.7 *Data storage.*

Data on all research patients (3611) was entered onto a customised database in the Medical Data Index (PAS) at Cheltenham General Hospital and downloaded into SPSS* version 10 for data analysis as required.

3.3.2.8 *Cost-effectiveness analysis.*

Capital costs were collected from original invoices and accounts data from the Finance Department (Ophthalmology) East Gloucestershire NHS Trust. Equivalent annual costs were estimated using a discount rate of 6% on the basis of a 5-year life for cameras, a 3 year life for computers and training and a 10 year life for all other items. Consumables and office expenditure were assessed retrospectively from the Retinal Screening Department budget statements. Office overheads were calculated using figures provided by the Estates Department, East Gloucestershire NHS Trust. Costs incurred by the patient attending screening were collected by means of a questionnaire to 400 patients attending screening in 15 randomly selected GP practices (see Appendix 9 for sample questionnaire). The same questionnaire was used to assess the costs incurred by a random sample of patients attending screening sessions (mop-up clinics) at Eye Clinics at Cheltenham General Hospital and Gloucestershire Royal Hospital. Screener's transport costs were calculated per patient screened at each of the designated research practices by recording mileage costs and the number of patients screened per practice. All data relating to the effectiveness of the screening methods were taken from the

clinical study. Sensitivity and specificity calculations are based on comparisons with a reference standard of slit lamp biomicroscopy and direct ophthalmoscopy. Patients were graded on their worst eye and photographic images which were ungradeable were treated as screen positives as the patients would be referred for assessment.
The comparative costs and effects for the opportunistic screening service were modelled using data from various sources. An audit of general practices in Gloucestershire, carried out in 1996, provided information on the proportion of each screening method used. The sensitivity and specificity of the screening methods were taken from the literature[6] and the costs were a combination of local information and data from published sources.

3.3.2.9 *Statistical methods used.*

Data were entered onto a customised database in the Medical Data Index (PAS) at Cheltenham General Hospital and downloaded into SPSS* version 10 for data analysis as required.
Sensitivity, specificity, positive and negative predictive values, together with 95% confidence intervals (CI), were calculated for the following comparisons:

- Mydriatic photography compared with the reference standard examination.
- Non-mydriatic photography compared with the reference standard examination.
- Non-mydriatic photography compared with mydriatic photography.

The study was designed to measure the sensitivity and specificity of the method by comparison of the grading of approximately 1500 patients using mydriatic and non-mydriatic photography by a research fellow against the reference standard examination examination of an experienced ophthalmologist. Patients were graded according to the result for their worse eye.
The study was also designed for the technical failure rates and the positive test rates for the two methods to be calculated from the combination of the gradings of approximately 1500 patients by the research fellow and the gradings of approximately 2,150 patients by PS (patients whom he had not examined). Technical failure rates and their confidence intervals were calculated for mydriatic and non-mydriatic photography. The rates of referable DR for mydriatic and non-mydriatic photography (in those patients with assessable images) were compared using the McNemar test.
Mydriatic images from 410 patients graded by PS (to include 21% that had been graded by PS at first grading as referable retinopathy) were also graded by RM and by an

experienced grader Helen Lipinski (HL) from the Retinopathy Grading Centre (Imperial College) to test for inter-observer variability and re-graded by PS for intra-observer variability. For this study of inter-observer variability in grading, percentage agreements between pairs of observers were calculated, together with kappa scores (a measure of agreement between two observers over and above that to be expected by chance, varying from zero for chance agreement to one for complete agreement). It is acknowledged (as previously mentioned on page 112) that the value of kappa is affected by the percentage of referable retinopathy in the population tested.

3.4 Results from the main evaluation study (study 2).

3.4.1 *Technical failure rate and image quality.*

3650 patients were invited but images of 39 patients (from one practice) were excluded from the study because the images were accidentally captured in JPEG format instead of TIFF format. Technical failure rates (Table 5) were calculated for all 3611 patients in the study to provide narrower confidence intervals.

The technical failure rate for non-mydriatic photography was 19.7% (95% Confidence Interval 18.4 to 21.0%), a further 31.2% having a partially assessable image in one or both eyes. Full assessability of both eyes was achieved in only 48.0% of patients.

The technical failure rate for mydriatic photography was 3.7% (95% CI 3.1 to 4.3%); a further 15.5% of patients had a partially assessable image in one or both eyes. Full assessability of both eyes was achieved in 80.1% of patients.

A patient who had referable retinopathy in one eye and an unassessable image in the other was not regarded as a technical failure (1% of the non-mydriatic group and 0.7% of the mydriatic group).

Table 6 – Quality of Image.

Quality of Image
• Fully assessable - possible to see the small vessels of the temporal arcades with reasonable clarity. • Partially assessable - possible to see the large vessels of the temporal arcades with reasonable clarity. • Not assessable - the large vessels of the temporal arcades were blurred or >1/3rd of the picture was blurred unless sight threatening retinopathy was detected in the remainder.

Quality of Images	**Mydriatic**		**Non-Mydriatic**	
	Frequency	Percent	Frequency	Percent
Fully assessable both eyes	2884	80.1	1727	48
Fully + partially	307	8.5	468	13.0
Partially assessable both eyes	251	7.0	656	18.2
Fully + not assessable	55	1.5	99	2.4
Partially + not assessable	42	1.2	289	7.3
Not assessable both eyes	36	1.0	358	10
Not assessable + referable DR	27	0.7	37	1.0
Total graded	3602	100	3597	100
Missing forms	9		14	
Total	3611		3611	

3.4.2 *Sensitivity and specificity.*

Sensitivity and specificity rates were calculated against a reference standard of slit lamp biomicroscopy for 1549 patients in the mydriatic photography group, and 1542 of these patients were included in the non-mydriatic group (7 grading forms were absent). Patients were graded according to the result of their worse eye. Patients with technical failures in either eye were classed as test positive when calculating sensitivity and specificity (on the basis that they would be referred for further assessment). In the reference standard group the Ophthalmologist did not report any eyes as unassessable.

3.4.3 *1 x 45 degree field Non-Mydriatic Photography (table 6).*

Images of 321 patients were ungradeable in at least one eye and are included as test-positive. The sensitivity was 86.0% (95% CI 80.9 - 91.1%), the specificity was 76.7% (95% CI 74.5 – 78.9%).

The positive predictive value of the test was 32.7% (95% CI 28.4 – 37.0%). The negative predictive value of the test was 97.7% (95% CI 96.8 - 98.6%).

Table 7 – Non-mydriatic screening result versus reference standard result.

	Non-Mydriatic screening results				
Reference standard result	**Not assessable**	**No DR**	**Non referable DR**	**Referable DR**	**Total**
Not assessable					0
No DR	216	701	150	18	1085 70.4%
Non referable DR	54	71	123	30	278 18.0%
Referable DR	51	7	18	103	179 11.6%
Total	321 20.8%	779 50.5%	291 18.9%	151 9.8%	1542 100%

3.4.4 *2 x 45 degree field Mydriatic Photography (table 7).*

Images of 86 patients were ungradeable in at least one eye and are included as test-positive. The sensitivity achieved was 87.8% (95% CI 83.0 - 92.6%), the specificity was 86.1% (95% CI 84.2 – 87.8%).

The positive predictive value of the test was 45.4% (95% CI 40.2 – 50.6%). The negative predictive value of the test was 98.2% (95% CI 97.4 - 99%).

Table 8 – Mydriatic screening result versus reference standard result.

	Mydriatic screening results				
Reference standard result	**Not assessable**	**No DR**	**Non referable DR**	**Referable DR**	**Total**
Not assessable					0
No DR	68	689	285	47	1089 70.3%
Non referable DR	9	52	153	66	280 18.1%
Referable DR	9	6	16	149	180 11.6%
Total	86 5.6%	747 48.2%	454 29.3%	262 16.9%	1549 100%

There were a total of 23 patients whom RM graded as non referable STDR or no DR who were recorded as having Referable STDR on reference standard examination. Of these, 10 patients had had extensive laser treatment and one had had an old Central Retinal Vein Occlusion. The reference standard grade had either recorded small fibrosed regressed NVE or reduced VA likely to be caused by a diabetic macular problem.

There were 113 patients whom RM had graded as referable STDR who were recorded as non referable STDR or no DR on reference standard examination.

Common sources of error are shown in Table 9 below:

Table 9 - Common sources of error.

Number	Reference standard grade (PS)	Photographic grading (RM)
33	Drusen	Hard exudates < 1DD
24	Ma's < 1DD	Haemorrhage < 1DD
9	Non grouped exudates > 1DD	Group of exudates > 1DD
6	CRVO/BRVO	Multiple haemorrhages
4	Reflective retinas	Hard exudates < 1DD

RM was grading cautiously and it is possible that having an experienced secondary grader checking the images before referral could reduce the number of false positives in a screening programme.
There were 304 patients graded as non referable DR who had no DR on reference standard examination and the reasons for this are discussed in section 6.3 below.

3.4.5 *Time interval between grading the mydriatic and non-mydriatic photographs.*
RM graded the mydriatic images of 1549 patients and non-mydriatic images of the same 1549 patients with a time separation of 8 weeks. PS graded the mydriatic images of 2062 patients and non-mydriatic images of the same 2062 patients with a time separation of 61 weeks and then repeated grading the mydriatic images of 410 of these patients (pre-selected with 21% referable DR) after a further time separation of 32 weeks. It is unlikely with these time separations, and the fact that PS was also grading 160 patients per week at that time for the Gloucestershire screening programme, that there would have been any memory effect.

3.4.6 *Comparison of the detection of referable DR between methods.*
Of the 3611 patients in the study, the calculation was based on 2860 patients with assessable images by both methods. The positive test rate for mydriatic photography was 13.5% and for non-mydriatic photography was 10.6%, the difference being 2.9% ($p< 0.001$).

3.4.7 *Comparison of positive test rates between methods.*
For all patients the positive test rates of the two methods were 14.8% for mydriatic photography and 8.5% for non-mydriatic photography ($p< 0.001$) as shown in Table 10 below:

Table 10 - Comparison of positive test rates between methods.

		Mydriatic referable STDR		
		No	Yes	Total
Non-mydriatic referable STDR	No	3037	259	3296 91.5%
	Yes	34	274	308 8.5%
	Total	3071 85.2%	533 14.8%	3604 100%

Of the 3611 patients in the study, 7 forms were missing and hence the calculation was based on 3604 patients.

3.4.8 *Referral rate and patients under ophthalmological care.*

In Gloucestershire the number of study patients already under the care of an Ophthalmologist at the time of screening was 389 (10.8% of 3611). Of these, 7 patients (0.1%) had their management altered by screening i.e. their appointments were brought forward.

The referral rate from mydriatic digital photography would have been 18.5% of the whole study population of 3611 patients (15.4% of 2042 patients' digital images graded by PS and 22.5% of the 1569 graded by RM). If one does not include patients already under the care of an Ophthalmologist, the referral rate from mydriatic digital photography was 12.2% of the whole study population.

3.4.9 *Type of Diabetes.*

3610 study patients: 16.5% Type 1, 81.6% Type 2 and 1.9% not known.

1549 reference standard group: 15.3% Type 1, 82.7% Type 2 and 2.0% unknown.

3.4.10 *Gender of study patients.*

3610 study patients: 55% male, 45% female.

1549 reference standard group: 55.2% male, 44.8% female.

3.4.11 *Grades of retinopathy.*

Table 11 shows the grades of retinopathy given to patients by the Ophthalmologist's reference standard examination compared to grading of the two field mydriatic digital

images. The results are based on the retinopathy result in the worst eye and if only one eye is gradeable the result is included:

Table 11 – Grades of retinopathy given by RM compared to reference standard.

Grade	% given by reference standard examination	% given by grading of digital photographic images in the same group of patients(RM)
Ungradeable in both eyes	0%	1.7%
No DR	70.3%	50.2%
Minimal NPDR	3.6%	14.9%
Mild NPDR	14.4%	16.0%
Stable treated DR	0.1%	0.3%
Maculopathy	6.8%	12.5%
Moderate/severe NPDR	2.8%	1.7%
Proliferative DR	1.7%	2.6%
Advanced DR	0.3%	0.1%
Total	100%	100%

The most obvious difference between the groups is the difference in the minimal group of 3.6% in the reference standard group and 14.9% in the same patients graded by RM.

Table 12 shows the grades given by PS to the other 2062 patients in the study and compares it to the percentages that one might expect from his reference standard examinations on a separate group of 1549 patients.

Table 12 Grades of retinopathy given by PS compared to the percentage expected from the reference standard examinations.

Grade	% expected from reference standard examinations	% given by grading of digital photographic images in 2062 other patients(PS)
Ungradeable in both eyes	0%	0.4%
No DR	70.3%	53.5%
Minimal NPDR	3.6%	16.0%
Mild NPDR	14.4%	16.7%
Stable treated DR	0.1%	0.3%
Maculopathy	6.8%	7.7%
Moderate/severe NPDR	2.8%	3.7%
Proliferative DR	1.7%	1.6%
Advanced DR	0.3%	0.2%
Total	100%	100%

The most obvious difference between the two groups is again the difference in the minimal group of 3.6% in the reference standard group and 16% in the other group of 2062 patients graded by PS.

The minimal group is defined as < 5 microaneurysms > 1DD from the macular centre or 1 haemorrhage > 1DD from the macular centre.

These results suggest that, although the results are good for the detection of referable STDR, the image resolution is not adequate to detect the microaneurysms or occasional small haemorrhage in the minimal group. This has lead to overgrading in this group. (N.B. A new grade 'stable treated DR' has been introduced to describe those patients recorded on the form as having had extensive laser treatment and no other retinopathy was recorded.)

3.4.12 *Coverage.*

An average of 74% of patients on GP registers attended for screening throughout the Gloucestershire practices. It is possible that the 26% not taking up the invite may have a higher incidence of referable DR than those who attended but this would not have

altered the sensitivity and specificity results of the method. Reference standard assessment was achieved in 98.1% of the target population who attended for screening when PS was available (1549 of 1579 study patients). 30 patients were excluded – the most common reason was an inability to climb stairs to the room allocated to PS (9) and refusal of dilation because the patient was driving (8). A further 13 patients were excluded from the study for the reasons shown in Table 13 below.

Table 13 - Reasons for exclusion from the study.

Number	*Reason*
9	***PS was in an upstairs room and patients could not climb the stairs.***
8	***Were not dilated because driving would have been unsafe or they were within 2 weeks of cataract surgery.***
4	***Learning difficulties – co-operation impossible.***
3	***Allergy to Tropicamide.***
3	***Patients confused due to dementia.***
1	***Refused to sign the consent.***
2	Disabled and could not get chin on the chin rest – one of these patients was found to have sight-threatening maculopathy by the screener's direct ophthalmoscopy but was excluded from the study due to lack of photographs.

3.4.13 *Added value of ophthalmoscopy and extra fields.*

Of the 3611 patients photographed there were 36 patients with unassessable images in both eyes. Of these 36 patients direct ophthalmoscopy prevented an inappropriate referral in only one, because the screener was confident that there was no diabetic retinopathy present and anterior segment views helped to diagnose the reason for unassessable images in 22 patients. In the remaining 3575 patients the screener's comments altered the grade of retinopathy in 33 patients, but in no patient did this change the diagnostic category into one requiring referral. Hence, technician ophthalmoscopy did not affect sensitivity and specificity. One patient, who was not included in the study because a physical handicap made digital photography impossible, was correctly identified as having referable retinopathy by the technician direct ophthalmoscopy. Anterior segment views helped to diagnose cataract in 575 patients

and extra retinal fields helped to diagnose other ocular conditions in 101 patients (e.g. naevi).

The results are shown in Tables 14-17.

Table 14 Results in patients with **ungradeable** images in both eyes (n=36).

	Patient results affected by ophthalmoscopy	
	Number	**Percent**
Extra fields altered diagnosis of other lesions (ophthalmoscopy determined extra fields)	1	0.03%
Screener's comments altered diagnosis of other lesions	33	0.9%
Extra fields altered grade of DR (ophthalmoscopy determined extra fields)	0	0%
Screener's comments altered grade of DR	3	0.05%

Table 15 Results for **all** patients (n=3611).

	Patient results affected by ophthalmoscopy	
	Number	**Percent**
Extra fields altered diagnosis of other lesions (ophthalmoscopy determined extra fields)	6	0.1%
Screener's comments altered diagnosis of other lesions	289	8%
Extra fields altered grade of DR (ophthalmoscopy determined extra fields)	1	0.03%
Screener's comments altered grade of DR	33	0.9%

Table 16 Results in patients with ungradeable images (n=36).

	Patient results affected by extra fields	
	Number	**Percent**
Extra fields altered diagnosis of other lesions	22	61.1%

Table 17 Results for all patients (n=3611).

	Patient results affected by extra fields	
	Number	**Percent**
Extra fields altered diagnosis of other lesions	676	18.7%
Extra fields altered grade of DR	11	0.3%

3.4.14 *Added value of Logmar Visual Acuity Measurement in detection of Diabetic maculopathy.*

Analysis of Visual Acuity in relation to diabetic maculopathy showed that:

- 36.0% of eyes with referable maculopathy and 12.6% of eyes without maculopathy had a Logmar visual acuity ≥ 0.3 i.e. VA $\leq 6/12$ ($p < 0.001$).

- 16.8% of all eyes with a visual acuity ≥ 0.3 had diabetic maculopathy.

Analysis of Visual Acuity in relation to age showed that:

- In patients over 70 yrs, 310 eyes (24.6% of 1259) had a VA ≥ 0.3.

Analysis of Visual Acuity in relation to age and different pathologies showed that:

- Of these 310 eyes in patients over 70 yrs, only 13.5% had diabetic maculopathy but 47.4% of them had cataract, 28.9% had Age Related Macular Degeneration (ARMD) and 17.9% had a combination of cataract and ARMD.

- In patients under 70 yrs, 125 eyes (6.9% of 1822) had a VA ≥ 0.3 and, of these, 24.8% had diabetic maculopathy.

3.4.15 *Age of study patients.*

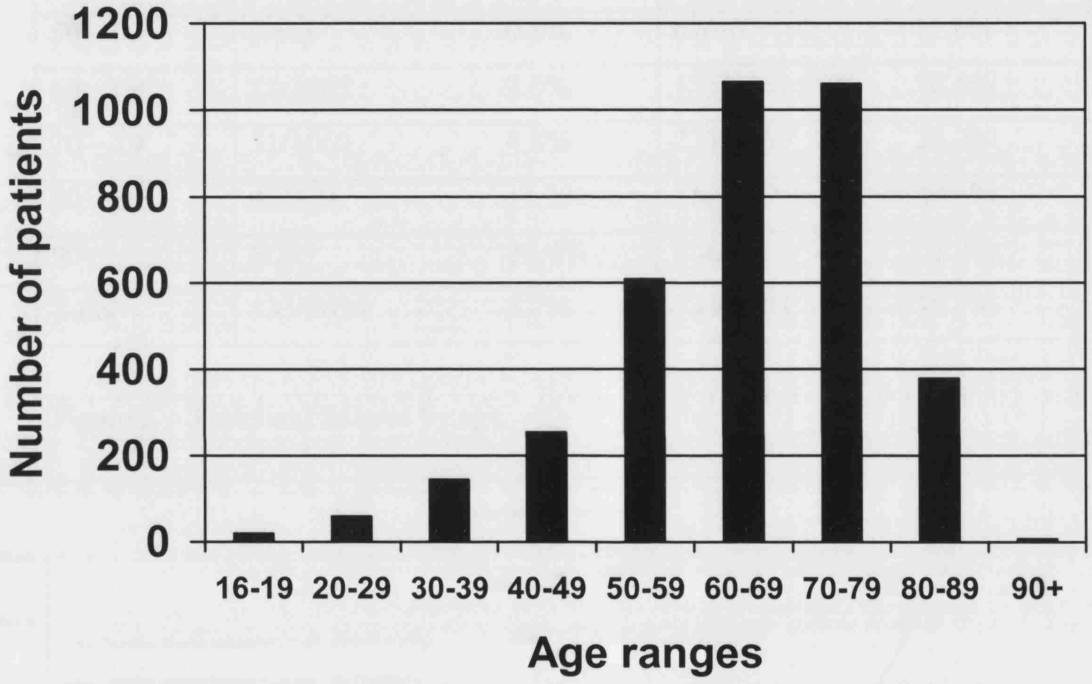
The mean age of the patients was 65yrs.

The age distribution of patients in this study was 19 (0.5%,16-19), 59 (1.6%, 20-29), 144 (4.0%, 30-39), 254 (7.0%, 40-49), 608 (16.8%, 50-59), 1065 (29.5%, 60-69), 1060 (29.4%, 70-79), 379 (10.5%, 80-89) and 22 (0.6%, 90+).

The subgroup who had the reference standard examination had very similar age distribution of 8 (0.5%, 16-19), 19 (1.2%, 20-29), 63 (4.1%, 30-39), 118 (7.6%, 40-49), 256 (16.5%, 50-59), 449 (29.0%, 60-69), 464 (30.0%, 70-79), 161 (10.4%, 80-89) and 11 (0.7%, 90+).

The age distribution of the whole study population is shown in the following:

Figure 1 – Age of Study Patient.

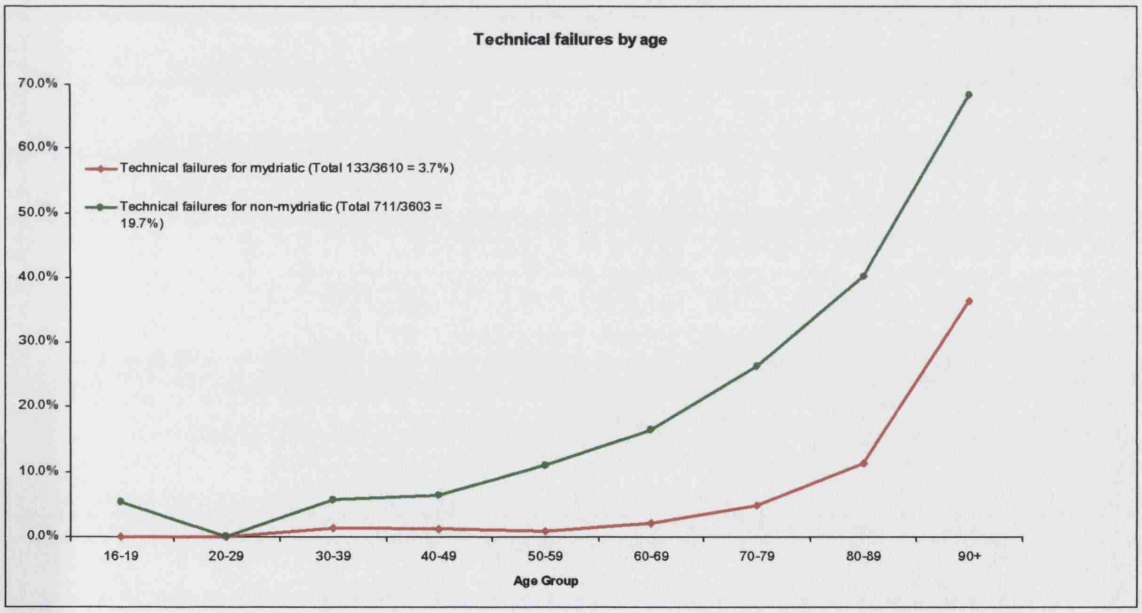


3.4.16 *Technical failure rate and age.*

Table 18 - Technical failure rate and age for non-mydriatic & mydriatic photography.

Age Group	Technical failures for mydriatic		Technical failures for non-mydriatic	
16 – 19	0/19	0.0%	1/19	5.3%
20 – 29	0/59	0.0%	0/59	0.0%
30 – 39	2/144	1.4%	8/143	5.6%
40 – 49	3/254	1.2%	16/254	6.3%
50 – 59	5/608	0.8%	67/607	11.0%
60 – 69	21/1065	2.0%	175/1061	16.5%
70 – 79	51/1060	4.8%	277/1059	26.2%
80 – 89	43/379	11.3%	152/379	40.1%
90+	8/22	36.4%	15/22	68.2%
Total	133/3610	3.7%	711/3603	19.7%

Figure 2 – Technical failures by age.



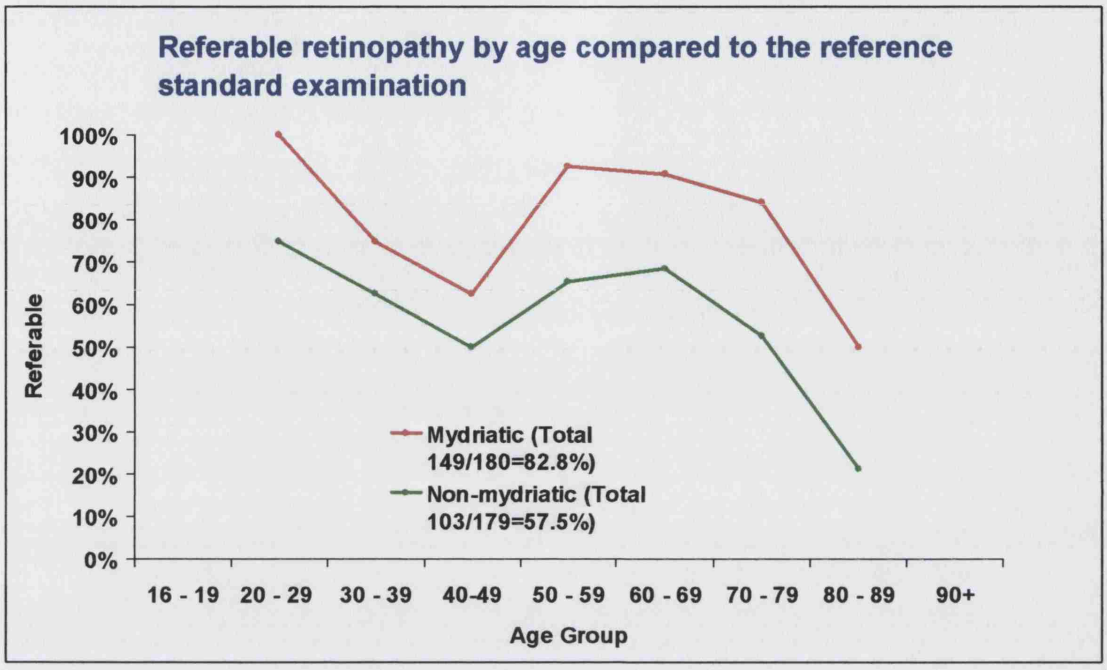
3.4.17 *Detection of referable retinopathy in different age ranges.*

In the 1549 reference standard group, levels of detection of referable diabetic retinopathy (DR) were 82.8% for the mydriatic group and 57.5% for the non-mydriatic group. Analysing the non-mydriatic figures in 10 year age groups, the younger age groups had significantly better image quality results but the only age groups detecting greater than 75% referable DR were those under 30 years of age and this fell to 21.4% in those over 80.

Table 19 Detection of referable retinopathy in different age ranges for non-mydriatic and mydriatic photography.

Age Group	Detection of referable retinopathy found on reference standard examination			
	Mydriatic		Non-mydriatic	
16 – 19	0/0		0/0	
20 – 29	4/4	100%	3/4	75%
30 – 39	6/8	75%	5/8	62.5%
40 – 49	10/16	62.5%	8/16	50%
50 – 59	25/27	92.6%	17/26	65.4%
60 – 69	49/54	90.7%	37/54	68.5%
70 – 79	48/57	84.2%	30/57	52.6%
80 – 89	7/14	50.0%	3/14	21.4%
90+	0/0		0/0	
Total	149/180	82.8%	103/179	57.5%

Figure 3 - Referable retinopathy by age compared to the reference standard examination.



3.4.18 *Duration of diabetes.*

For the 3602 of the study population that information was available, the duration of diabetes was: 0-4 yrs 1501 (41.7%), 5-9 yrs 943 (26.2%), 10-14 yrs 495 (13.7%), 15-19 yrs 275 (7.6%) and 20 + yrs 388 (10.8%).

For the subgroup of 1544 of the reference standard subgroup that information was available, the duration of diabetes was: 0-4 yrs 638 (41.3%), 5-9 yrs 413 (26.7%), 10-14 yrs 213 (13.8%), 15-19 yrs 117 (7.6%) and 20 + yrs 163 (10.6%).

3.4.19 *Logistic regression analysis of mydriatic or non-mydriatic technical failure rate versus age and versus duration of diabetes for the full study population.*

Because there was an association between technical failure and age and there was an association between age and duration of diabetes, a logistic regression analysis was undertaken to see if the associations were independent of each other.

For non-mydriatic photography the odds of having one eye unassessable increased by 2.6% (CI 1.6-3.7%) for each extra year since diagnosis, irrespective of age, and by 5.8% (CI 5.0-6.7%) for every extra year of age, irrespective of years since diagnosis.

For mydriatic photography the odds of having one eye unassessable increased by 4.1% (CI 2.7-5.7%) for each extra year since diagnosis irrespective of age and by 8.4% (CI 5.0-6.7%) for each extra year of age, irrespective of years since diagnosis.
The analysis showed that both age and years since diagnosis contributed to the odds of having an unassessable image in one eye.

3.4.20 *Regradings for inter and intra-observer variability.*
410 patients (2-field digital of both eyes) were graded twice by PS, with an interval between grading of greater than 1 year. PS was the Ophthalmologist who graded the 2,062 non-reference Standard Patients. The 410 patients were also graded once by RM (Specialist Registrar in Ophthalmology who graded the 1549 Reference Standard Patients) and once by HL (Senior Grader at the Retinopathy Grading Centre).
The Gloucestershire grading form was used by all three graders in order to measure inter-observer variability. Sight threatening diabetic retinopathy was defined as grades 3 to 6 on the form and assessed per eye.
There was a time difference of 18 months between the grading of PS1 and PS2.
The results are shown in Tables 20-25. The totals are slightly different in the tables because of a small number of missing forms from HL and RM.
For inter-observer variability, the kappa values for sight threatening retinopathy showed a good measure of agreement of 0.690 (standard error 0.033), 0.749 (standard error 0.030) and 0.673 (standard error 0.035) for RM against PS1, PS2 and HL.
For intra-observer variability, the kappa values for sight threatening retinopathy showed a good measure of agreement of 0.780 (standard error 0.028) for PS1 against PS2.

In view of the overgrading of the minimal group in the study, the percentage of images graded as minimal NPDR was compared between the three graders. The results were RM 7.3%, PS1 11.4%, HL 12.2% and PS2 was 4.7%. These results suggest that PS graded many fewer in the minimal group as he became more experienced at grading digital images (he had graded approximately 7000 patient's images during the 18 month period). RM had graded all 1549 mydriatic and non-mydriatic images in the reference standard patients before commencing these gradings. HL is an experienced grader using 35 mm film but is less experienced with digital images.

Table 20 RM V PS 1.

		PS 1		
		Not sight threatening	**Sight threatening**	**Total**
RM	**Not sight threatening**	619	56	675
	Sight threatening	20	112	132
	Total	639	168	807

RM V PS 1	Value	Standard Error
Measure of Agreement Kappa	0.690	0.033

Table 21 RM V PS 2.

		PS 2		
		Not sight threatening	**Sight threatening**	**Total**
RM	**Not sight threatening**	622	47	669
	Sight threatening	14	118	132
	Total	636	165	801

RM V PS 2	Value	Standard Error
Measure of Agreement Kappa	0.749	0.030

Table 22 PS 1 V HL.

		HL		
		Not sight threatening	**Sight threatening**	**Total**
PS 1	**Not sight threatening**	616	21	637
	Sight threatening	49	120	169
	Total	665	141	806

PS 1 V HL	Value	Standard Error
Measure of Agreement Kappa	0.721	0.031

Table 23 PS 2 V HL.

		HL		
		Not sight threatening	**Sight threatening**	**Total**
PS 2	**Not sight threatening**	617	19	636
	Sight threatening	44	121	165
	Total	661	140	801

PS 2 V HL	Value	Standard Error
Measure of Agreement Kappa	0.745	0.030

Table 24 RM V HL.

		HL		
		Not sight threatening	**Sight threatening**	**Total**
RM	**Not sight threatening**	635	41	676
	Sight threatening	33	99	132
	Total	668	140	808

RM V HL	Value	Standard Error
Measure of Agreement Kappa	0.673	0.035

Table 25 PS 1 V PS 2.

		PS 2		
		Not sight threatening	**Sight threatening**	**Total**
PS 1	**Not sight threatening**	606	28	634
	Sight threatening	30	137	167
	Total	636	165	801

PS 1 V PS 2	Value	Standard Error
Measure of Agreement Kappa	0.780	0.028

3.5 Economic results from study 2.

3.5.1 *Screening programme costs.*

Costs for the systematic screening programme were estimated in 1998/9 prices and broken down into the administrative costs of running the programme and issuing invitations (£3.13 per person invited for screening), capital costs (£7.44 per person screened) and running costs (£18.11 per person screened). The cost of assessment for screen positive cases is taken as the cost of a first ophthalmology outpatient appointment. (National Reference Cost 1999/2000 deflated to 1998/9 prices using Health Service Cost Index).

Table 26 Costs of screening programme (1998/9 prices).

Screening costs		Annual cost £	
Invitation and administration			
Staff cost		14208	
Consumables		4900	
Sub total		19108	
Cost per person invited (6100 per annum).			3.13
Screening *and grading*			
2 cameras and trolleys	69795 over 5 years	16569	
Computers, software etc	39383 over 3 years	14734	
Office conversion and minor equipment	13174 over 10 years	1790	
Training	1500 over 3 years	561	
Sub total		33654	
Cost per person screened (4524 per annum)			7.44
Van lease (2) and petrol		9192	
Warranties and software support		4872	
2 screeners		44880	
Grading (medical and non-medical staff)		22712	
Consumables (mydriatic)		280	
Sub total		81936	
Cost per person screened (4524 per annum)			18.11

3.5.2 *Screening using mydriatic digital retinal photography.*

The cost per true positive detected has been calculated on the basis of a cohort of 1000 patients invited to screening. The take up rate for screening was 74%, giving 740 patients attending for screening and grading. The prevalence of STDR in the screened patients was 11.6%, based on the reference standard examination. (This figure includes patients already under the care of an Ophthalmologist). This translates into 86 patients out of 740 with STDR and 654 without STDR. With a sensitivity of 87.8% (95%CI;

83.0 – 92.6), 76 (71 – 80) of the positive cases will be detected and recalled for assessment. With a specificity of 86.0% (95%CI; 84.2 – 87.8), 92 (80 - 103) patients without STDR will be recalled for assessment, giving a total for assessment of 168 (151 – 183). The central estimate of cost per true positive detected is £429 (range £394 – £472) (see Table 27).

Table 27 Costs and effectiveness for mydriatic screening programme (1998/9 prices).

	Cost per patient £	Number of patients	Total cost £
Invitation and administration	3.13	1000	3130
Screening and grading	25.55	740	18907
Assessment	63.00	168	10584
(range)		(151 – 183)	(9513 – 11529)
Total			32621
(range)			(31550 – 33566)
True positives detected		76	
(range)		(71 – 80)	
Cost per true positive detected			429
(range)			(394 – 473)

3.5.3 *Screening using non-mydriatic digital retinal photography.*

Comparable results are shown in Table 28 for the non-mydriatic screening. With a sensitivity of 86.0% (95%CI; 80.9 – 91.1), 74 (70-78) of the positive cases will be detected and recalled for assessment. With a specificity of 76.7% (95%CI; 74.5 – 78.9), 152 (138 –167) patients without STDR will be recalled for assessment, giving a total for assessment of 226 (208 – 245). The cost per true positive appears to be higher for non-mydriatic screening with a best estimate of £490 (range £450 – £535) but the range of cost estimates, constructed from the confidence intervals around sensitivity and

specificity estimates, overlap. No allowance has been made for the possible higher throughput that may be achieved without the administration of drops. In order for the cost per true positive to be equal with and without mydriasis, the cost of screening and grading without mydriasis would have to fall to £19.43. As grading costs will not be affected by increased screening throughput, the necessary saving translates into a 42% increase in screening throughput.

Table 28 Costs and effectiveness for non-mydriatic screening programme (1998/9 prices).

	Cost per patient £	Number of patients	Total cost £
Invitation and administration	3.13	1000	3130
Screening and grading	25.49	740	18863
Assessment	63.00	226	14238
(range)		(208 – 245)	(13104 – 15435)
Total			36231
(range)			(35097 – 37428)
True positives detected		74	
(range)		(70 –78)	
Cost per true positive detected			490
(range)			(450 –535)

3.5.4 *Opportunistic screening.*

The comparative costs and effectiveness of continuing with the opportunistic arrangements for screening that existed prior to the introduction of the screening programme were calculated using the distribution of screening methods identified from a survey of general practices in 1996 and cost and effectiveness data taken from the literature. The distribution and cost for each screening method is shown in Table 29. The hospital screening cost is 1/3 of the cost for a general medicine follow up visit, assuming that the screening takes place as part of an annual check up for diabetic

patients. The GP cost is based on 5 mins per screen and includes practice nurse costs[273]. The other screening was all carried out by opticians or Optometrists and is costed at the standard sight test fee.

Table 29 Distribution of screening methods across patients (per 1000 patients).

Screening mode	Hospital or shared care	GP care	Total	Cost per screen 1998/9 prices	Cost
Hospital – physician	407	20	427	24	10248
GP		259	259	9.55	2473
Other on GP premises		6	6	14.57	87
Other (OMP, optician)		180	180	14.57	2623
None		128	128		
Total	407	593			15431
Cost per screen (n=872)					17.69

Effectiveness estimates were taken from a recent review[6]. It should be noted that the comparison of these results with the study reported here should be interpreted with caution, as the treatment of ungradeable images may differ. The best estimate of true positives given is based on the highest mean sensitivity result reported or the only result if only one study was available. The range is based on the reported confidence intervals. Similarly, the best estimate of false positives requiring assessment is based on the highest mean specificity and the range is based on confidence intervals. The audit data did not provide annual take up rates but 25% of patients had not been examined in the past 15 months. For the purposes of comparison, therefore, all the figures were adjusted to the same take up rate as the organised programme (74%).

Table 30 Estimated costs for opportunistic screening 1998/9 prices.

	Cost per patient	Number of patients	Total cost
	£		£
Screening	17.69	740	13091
Assessment	63.00	99	6237
(range)		(57 – 129)	(3591 – 8127)
Total			19328
			(16682 – 21218)
True positives detected (best estimate)		61	
(range)		(38 – 72)	
Cost per true positive detected (best estimate)			317
(range)			(232 – 558)

3.5.5 *Comparison of cost-effectiveness.*

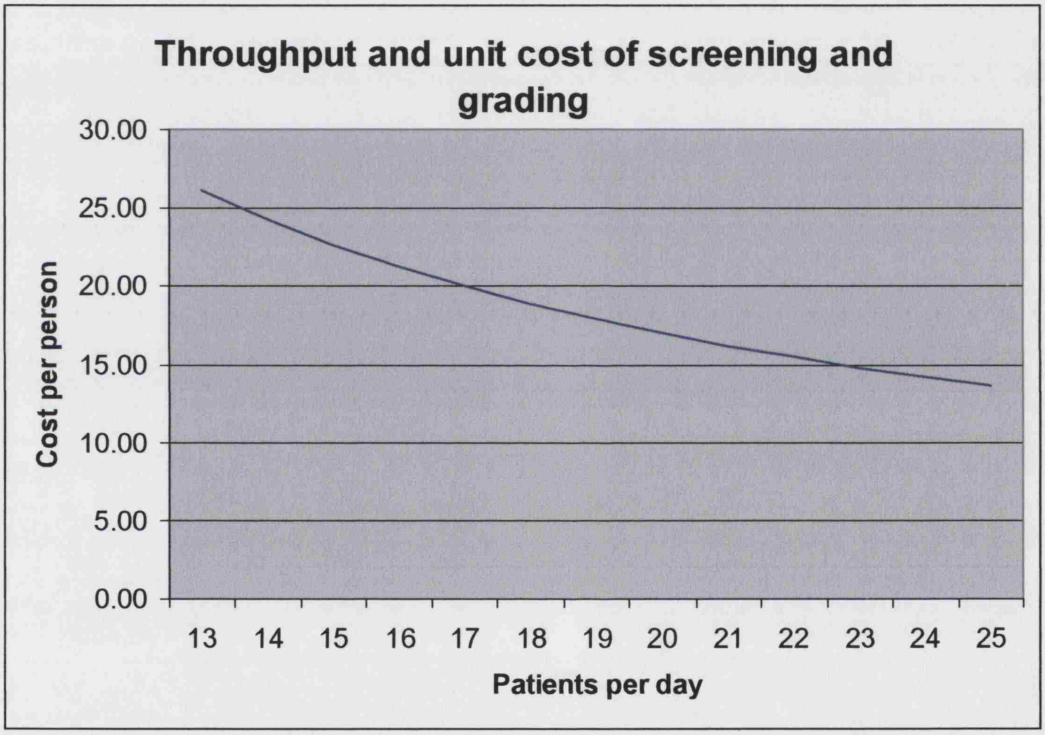
The best estimate of cost per case detected for opportunistic screening is £317, and this is less than the estimates for the systematic screening programme. However, this result is based on both lower costs and lower effectiveness. One technology is only considered to be dominant over another when it has both lower costs and better effectiveness. When this is not the case, it is important to consider the incremental cost per case detected for the more effective programme. The cost per additional true positive detected by organised screening with mydriatic photography is £886 (£32621 – £19328) / (76 – 61).

3.5.6 *Sensitivity analysis.*

The results reported above have included ranges based on the confidence intervals around the sensitivity and specificity of the screening methods. The other factor that has a major impact on cost and, hence, on the cost-effectiveness of the screening

programme is the throughput of patients. The main results reported above are based on 13.3 patients per day. If the planning figure of 17 per day used in the National Screening Committee costing was achieved then the cost would fall to £19.99 as shown in the figure (£375 per true positive). If 20 patients could be seen per day, without additional staffing, the cost for screening and assessment would fall further to £16.99 with a cost per true positive of £346. The effect of these improvements in throughput would be to reduce the incremental cost per case detected for the organised screening programme to £612 (17 patients per day) and £464 (20 patients) respectively.

Figure 4 – Throughput and unit cost of screening and grading.



3.5.7 *Patient costs.*

Costs were collected for the time and travel incurred by patients and any companions attending for screening. The average cost derived from a sample of 398 patients was £12.30 (SD 15.09). The distribution was heavily skewed by a small number of patients incurring very high time costs. The median cost was £8.45. Patients who were unable to attend for screening at the GP premises were offered appointments at occasional hospital based screening sessions. Costs collected from 15 such patients also showed a skewed distribution with a mean of £19.89 (SD 20.14) and a median of £14.44. Based

on this small sample, it does appear that the mobile screening service is less costly for patients than a hospital based service and this may be an important factor in the take up of the service. Under the opportunistic screening arrangements, almost half of patients were screened at hospital. These visits may have been combined with other diabetic services.

3.6 Discussion.

3.6.1 *Comparison with other studies in the literature of mydriatic digital photography in diabetic eye screening.*

Diabetic retinopathy is the single largest cause of registered blindness in England and Wales amongst people of working age.[43] In 1997 the British Diabetic Association (now Diabetes UK) set a standard[226] for retinopathy screening of 80% sensitivity, 95% specificity and a technical failure rate of < 5%. A recent systematic review[6] has evaluated a number of photographic screening studies, mostly using 35mm or Polaroid film. Only a small number of these studies included a reference standard of seven field stereo photography, which has been used in a number of landmark epidemiological studies[63-66 68 71 72 74 76 116 117 274] of diabetic retinopathy, or slit lamp bio-microscopy by an experienced Ophthalmologist. The latter is another widely accepted method for validating screening methods.[138 139]

Digital imaging retinal photography has shown promising results in a number of small photographic studies[168 170-174 176 178 180-182 186 200] with under 150 patients, two between 150 and 300 patients[179 183] and in two larger screening studies[158 275] of over 500 patients. In table 52 (and figure 5) the current study has been compared with five studies that used either of the above reference standards, the majority having sensitivities between 80% and 90%. The study by Stellingwerf et al [156] reported a higher sensitivity of 95% but had a younger age group of patients (average 51 yr.), and their definition of sight-threatening retinopathy included mild retinopathy with any hard or soft exudates in either fundus. These are relatively easy lesions to see on a digital photograph, and are not widely regarded to be sight threatening if not in the macular region. The Olson[158] study reported a sensitivity of 93% with two 50 degree field red free digital images. The digital study by Taylor et al[145] reported a sensitivity of 85%, improving to 95% with direct ophthalmoscopy, and a specificity of 97%. However, this study had relatively small numbers of referable retinopathy (20) in their reference standard group. The current study was unable to demonstrate any alteration in sensitivity or specificity

from the addition of technician direct ophthalmoscopy. Previous studies have suggested that technician direct ophthalmoscopy can improve the sensitivities and specificities of detection of sight threatening retinopathy[145 151]. It is recognised that our nurse technicians were inexperienced but they had received a six week period of training that included direct ophthalmoscopy prior to commencing the job. In a National Screening Programme, many technicians performing this task will be relatively inexperienced compared to those technicians or Optometrists from studies that have shown the beneficial effect of direct ophthalmoscopy.

Both this study, and the Liverpool Diabetic Eye Study[139] reported lower specificities than most of the other studies because of a difference in analytical methods – these studies included technical failures as test positive whereas the other studies excluded them from the analysis. This does call into question whether the 1997 BDA recommendations[226] are achievable when technical failures are included as test positive. The studies by Pugh[138], Taylor[145], Stellingwerf[156] and Olson[158] study did not include technical failures as test positive.

In the current study 10 of the 23 false negatives were patients with a past history of extensive laser treatment. Of the 113 false positives, common sources of discrepancy were drusen being graded as hard exudates (33), microaneurysms being graded as haemorrhages (24) and non-grouped exudates being graded as groups of exudates > 1DD from the foveola (9). This was considered to be the reason for the difference in referral rates of 15.4% of 2042 patients' digital images graded by PS compared with 22.5% of the 1569 graded by RM. It is likely that substantially better concordance could be achieved between graders and a reference standard examination with better training and feedback for graders, and improvement to interpretation of definitions of referable diabetic retinopathy. The sensitivity and specificity data show that 199 patients would have been unnecessarily referred following mydriatic photography (6.9% of those with no STDR, but 57.2% of all referrals).

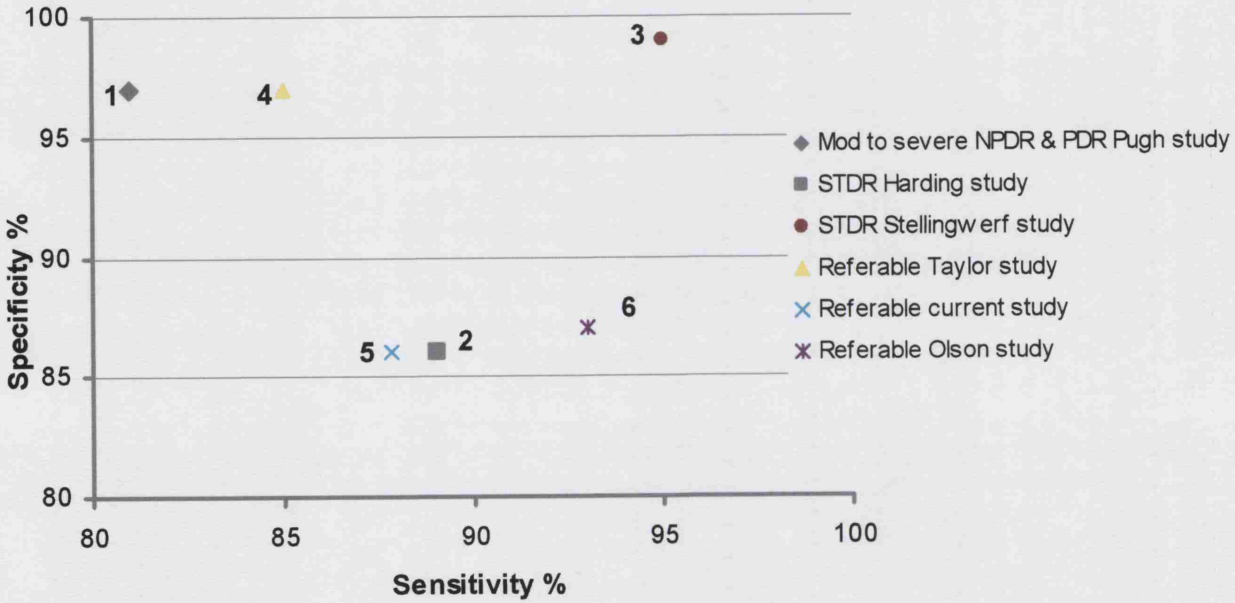
In this study there was a 26% non-attendance rate for screening. This figure compares well with other methods for the first round of a screening programme. Further studies need to be undertaken on methods to improve this rate and identify reasons for non-attendance.

The Sony Digital Camera used in this study has a resolution (768 x 568 pixels) below the level (1,365 x 1,000) subsequently recommended by the National Screening

Committee (NSC). Further studies are required to determine whether higher resolution cameras can achieve an improvement in sensitivity and specificity.

The NSC has recommended the introduction of a National Screening Programme for the detection of sight threatening diabetic retinopathy and their preferred model is mydriatic digital photography[8 9 253]. The National Service Framework Delivery Strategy[14] has recommended that by 2006, a minimum of 80% of people with diabetes are to be offered screening for the early detection of diabetic retinopathy as part of a systematic programme that meets national standards, rising to 100% coverage of those at risk of retinopathy by the end of 2007. The National Institute for Clinical Excellence (NICE) has produced a report[13], which recommends annual screening using mydriatic retinal photography. However, the Health Technology Board for Scotland (HTBS)[12] recommended a three stage screening procedure, in which the first stage should be one-field non-mydriatic digital photography, with mydriatic photography used for failures of non-mydriatic photography and slit-lamp biomicroscopy for failures of both photographic methods. The National Screening Programme in Scotland is being implemented using this procedure.

Figure 5. Sensitivity and Specificity results of current project within context of other recent published findings.



See table 31 for key.

Table 31

Study	Type of DR identified	*Read by*	TYPE AND FILM	*Reference standard*	Total number of patients (number reference examination)	Reference
1	Moderate to severe NPDR & PDR	Independent grader	3 x 45 degree mydriatic 35 mm colour slides	Stereoscopic 7-field retinal photography	n = 352 (351)	Pugh et al 1993
2	Sight Threatening	Ophthalmologist clinical assistant	3 x 45 degree mydriatic 35 mm colour slides	Slit lamp biomicroscopy by retinal specialist	n = 358 (326)	Harding et al 1995
3	Sight Threatening	Retinal specialist	2 x 45 degree mydriatic 35 mm colour slides	Slit lamp biomicroscopy by one of 6 Ophthalmologists	n = 469 (469)	Stellingwerf et al 2001
4	Referable	Experienced grader	1 x 45 degree mydriatic digital colour	Stereoscopic 7-field retinal photography	n = 731 (118)	Taylor et al 1999
5	Referable	SPR Ophthalmology	2 x 45 degree mydriatic digital colour	Ophthalmologist slit lamp biomicroscopy	n = 3611 (1549)	Scanlon et al 2003
6	Referable	SPR Ophthalmology	2 x 50 degree mydriatic digital red free	Slit lamp biomicroscopy by retinal specialist	n = 586 (586)	Olson, Sharp et al 2003

3.6.2 *Discussion relating to mydriasis versus non-mydriasis in this study.*

Dr Peter Scanlon, gave the Health Technology Board for Scotland (HTBS) access to the dataset arising from this large study of a screening service in Gloucestershire during the final stages of the HTBS assessment. Their final report[12] in 2002 described an analysis of the first two stages of their recommended three-stage screening process using data from the Gloucestershire Diabetic Eye study (study 2 in this thesis). The analysis concluded that the data from this large population-based study suggest that the first two stages of the three-stage screening programme recommended by HTBS will be feasible and effective.

The HTBS analysis makes two basic assumptions.

1. That the results from grading one mydriatic 45 degree field would be equal to the results of grading two mydriatic 45 degree fields in those who were ungradeable on non-mydriatic image and needed dilating. In order to justify this assumption it quotes the work of Olson[158] and Sharp[15], who compared one red free 50 degree digital image with two red free 50 degree digital images.
2. It also assumes that the grading of quality of image by the primary screener will be consistently able to assess image quality and make a correct decision as to whether a diabetic person with a partially assessable or ungradeable image requires mydriasis. In a busy clinic this may not be as easy as assumed. The current study has shown that, not only is there a technical failure rate for non-mydriatic photography of 19.7%, but a further 31.2% having a partially assessable image in one or both eyes. Hence the primary screener will have to make a judgement of whether there is a partially assessable or ungradeable image in 52% of patients.

The HTBS report acknowledges the fact that age is quite a strong predictor of the need for mydriasis. However, it states that in an annual screening programme it is likely that the strongest predictor will be the need for mydriasis on the previous screening occasion. No evidence is given for this statement.

The current study shows a very strong correlation with age and a less strong correlation with duration of diabetes. For non-mydriatic photography the odds of having one eye unassessable increased by 5.8% (CI 5.0-6.7%) for every extra year of age, irrespective

of years since diagnosis and by 2.6% (CI 1.6-3.7%) for each extra year since diagnosis, irrespective of age.

Screening programmes in Northern Ireland have looked at the data from their own series of patients and have a policy of screening those < 50 without mydriasis and those ≥ 50 with mydriasis. The findings of the current study found technical failures for non-mydriatic photography in the 16 – 19 age group to be 5.3%, 20 – 29 age group to be 0.0%, 30 – 39 age group to be 5.6% and 40 – 49 age group to be 6.3%. Hence the Northern Irish approach does have a good evidence base by picking out the group who are at lowest risk of ungradeable images and some authors suggest are at greatest risk of blindness (e.g. MacCuish[2] and Jones[221]). If this was proven to attract the group of regular young non-attendees, it would certainly be an approach worth considering for the English programme.

3.6.3 *Discussion of the Economic aspects of the main evaluation study (study 2).*

James et al[249] have reported results for an organised screening programme using 35mm retinal photography and demonstrated this to be more cost-effective than the previous system of opportunistic screening (£209 per true positive compared with £289 (1996/7 prices)). Allowing for the difference in price bases, the screening costs in this study are still higher at £429 per true positive detected. The reasons for this are related to travelling and set up time, downloading and other administrative time and educational activities undertaken with patients. One advantage of digital imaging is that patients can be shown the images of their eyes and the effect of poor diabetic control can be discussed.

The organised screening programme was more expensive than the previous opportunistic arrangements but detected more cases of sight threatening diabetic retinopathy. The additional cost per additional case detected was £886. This cost could be reduced if higher throughput levels were achieved. However, significantly increasing the throughput would have the disadvantage of less time for patient education. The results presented here have been based on all cases of referable diabetic retinopathy detected and are equivalent to a first round or prevalence screen. The cost of detecting new or incident cases in later screening rounds will be much higher, although the screening results also altered the management of a small number of patients. Assuming an incidence of new cases of 1.5% and annual screening, subsequent screening rounds would produce costs of £2909 per true positive for

mydriatic digital imaging retinal photography and £2038 for opportunistic screening. The additional cost of detecting an additional case is estimated to be £6395.

The throughput in this study was low at approximately 13.3 patients per day. Higher throughputs of 17 patients per day have since been achieved in the Gloucestershire service.

4 Study 3.

4.1 Justification for the workload study (study 3).

In 2000, the National Screening Committee produced their recommendations[7-9] for a National Screening Programme and estimated the effect on treatment workload and associated costs. A workload study was necessary to test these hypotheses in an area that had an ad hoc screening service and was introducing the recommended model of digital photographic screening, as we were in Gloucestershire.

4.2 Aims and objectives.

4.2.1 Aim of the workload study (study 3).

- To determine how the workload of an Ophthalmology Department changes following the introduction of an organised retinal screening programme and the resource consequences.

4.3. Study Design and Methods.

4.3.1 Design and methods for the workload study (study 3).

4.3.1.2 *Design.*

A retrospective collection of data from the notes on diagnosis and management after electronic identification of diabetic patients attending by matching retinal screening numbers with eye clinic codes.

4.3.1.3 *Sample group.*

The sample group was all known diabetic subjects in Gloucestershire aged > 16yrs attending as new patients to eye clinics in Gloucestershire over 4 years. This case review covered the year before the introduction of screening, the two years of the first round of screening and first year of the second round of screening.

All diabetic subjects aged 16 yrs and over in Gloucestershire have been given a retinal screening number (this includes those responding and those not responding to the screening invitation). The source of the lists of diabetic subjects has been the diabetic registers of all of the 85 General Practices in Gloucestershire. These lists were collected just before the screening visit to these practices and 12,300 diabetic subjects in Gloucestershire were identified (2.6% of the population) in February 2001 and later 13,239 in October 2001. Patients with retinal screening numbers on the East Gloucestershire PAS system were matched against all new patient attendance at eye clinic codes on the same system in February 2001 and again in October 2001. For West Gloucestershire, all patients with retinal screening numbers were matched against all new patient attendance to West Gloucestershire Eye clinics using NHS number, surname, forename and DOB. The retrospective identification of these diabetic subjects attending was undertaken once the first round of screening had been completed and an accurate list of diabetic subjects aged > 16 years had been collected.

Exclusion criteria:
Those aged less than 16 years. We do not collect information on diabetic subjects under 16 years for our screening service at the present time. There are approximately 170 diabetic subjects in this age group who are under the care of Gloucestershire paediatricians and were not included.

4.3.1.4 *Justification of sample size.*
The number of diabetic subjects attending as new patients to eye clinics in Gloucestershire over a 3-year period was 2,700 and it was expected to be 3,600 for the 4 years when the data was collected in October 2001.
8566 Diabetic Subjects were screened in the first round of screening in Gloucestershire with 434 referred with sight-threatening diabetic retinopathy (STDR – 33 proliferative, 102 preproliferative and 299 maculopathy). Our previous study (study 1) showed a sensitivity of 88% in detection of STDR. It follows that a missed (false negative) might occur in 5 proliferative patients out of 8566 (0.06%) diabetics and in 41 maculopathy patients (0.48%). To identify these small numbers required looking at all 3600 records.

In this study complete coverage was intended and there was therefore no sampling.

4.3.2 *Methods.*

The medical records from all new diabetic referrals to Eye Outpatient Departments in Gloucestershire over four years were examined and the information in Appendix 10 was recorded. Further information was collected on specific subgroups of patients identified by this initial form.

The electronic screening records were checked to determine the dates of screening and the non-responders to the screening invitation.

4.3.2.1 *Economic design and methods.*

This study was designed to provide accurate information about the changes in workload that take place following the introduction of an organised screening programme. In addition to the data that have been collected on referral and treatment rates, there was existing information on the nature and coverage of the ad hoc screening carried out derived from a Primary Care Clinical Audit carried out in 1996. This provided a useful basis for extrapolating the results in Gloucestershire to other health authorities. An audit of laser treatment was conducted alongside the present study (see Appendix 11) and was used to estimate the resource consequences of treatment referrals.

Workloads were evaluated for each year of the four years of the study. The changes in workload identified from the case note review were used to estimate resource consequences. These were calculated first in terms of physical units of resource use, such as hours of staff time, outpatient time, laser treatment time, theatre time, numbers of inpatients days. The resource use associated with each activity or treatment was identified through discussion with nursing and medical staff and through observation. A schedule was drawn up specifying items such as the facilities required for the activity or treatment, staff involved and time taken, and consumables used. Financial information was obtained from published sources and from Gloucestershire Hospitals NHS Trust. (All costs were in 2002-3 prices). The costs that result are marginal costs; i.e. they relate to the direct consequences of changes in workload and do not include overhead costs where the change in workload is not of sufficient scale to affect overall hospital running costs. Sensitivity analysis was carried out using the average cost estimates from the NSC report, in order to test whether or not the results varied with the costing method applied.

4.4 Results from the workload study (study 3).

4.4.1 *The annual new diabetic referral rate to eye clinics in Gloucestershire over a 4 year period.*

Over the four year period 3877 people with diabetes were identified electronically as having attended Eye clinics in Gloucestershire as new patients (Table 31). This included patients who were already under the Eye clinic who attended as an emergency at a date between their booked appointments.

Table 32 - New Referrals in People with Diabetes.

Annual new diabetic referrals to eye clinics in Gloucestershire	East Glos attendances	West Glos attendances	Total attendances	Notes not examined
Year 1997 – 98	393	460	853	7
1998 –99	451	503	954	7
1999 –00	469	505	974	8
2000-01	483	568	1051	23
Total	1796	2036	3832	45

There has been a progressive rise in new patient attendances of people with diabetes in the eye clinic during the four years starting in 97-98 with annual rises from 853 to 954, 974 and 1051.

Of the 3877 patients attending Eye clinics it was possible to examine the notes of 3832 patients and extract information from the notes relating to the clinic attendance.

The analysis has therefore been confined to the 3832 patients whose notes were examined and has not included 45 patients over the four years whose notes were not obtainable (Table 32) or the 8 patients where no sign of a clinic appointment was found in the notes.

Table 33 - notes not examined.

East Glos notes not examined	West Glos notes not examined	Reason for notes not examined or included
12	5	Lost
8	7	Missing
8	5	Temporarily unavailable
28	17	Total = 45

During the first three years of screening by the Gloucestershire Diabetic Eye Screening Service (GDESS) there was a gradual increase in the numbers screened per annum from 4,157 to 4520 (Table 33).

Table 34 – Numbers screened by GDESS (bi-annual service).

Year 1998 –99	4157
1999 –00	4540
2000-01	4520
Total	13217

4.4.2 *The number of diabetic patients in the county – annual increases.*

In the 1996 Gloucestershire Audit there were 9566 people with diabetes identified in the county. After the first round of screening in October 2000 there were 11,909 identified. The following October 2001 there were 13,239 people with diabetes identified. This number has continued to rise at a rate of approximately 1,400 per annum and is now 15,433 in May 2003 (Table 34).

Table 35 – Number of adult diabetic persons in Gloucestershire (aged > 16yrs).

October 1996	9566
October 2000	11,909
October 2001	13,239
October 2002	14,443
May 2003	15,433

4.4.3 *The reason given for attendance.*

The commonest reasons for referral are reduced vision and retinopathy seen, which were two of the three options given. Although the numbers referred with reduced vision appear to have slightly reduced over the four years (288, 272, 232, 221), the numbers referred with retinopathy seen have shown a progressive rise (222, 328, 357, 364).

The number referred for an opinion about cataract appears to have increased a small amount (64, 57, 77, and 93).

The number referred for a glaucoma opinion appears to have remained fairly stable (57, 62, 61, and 68).

4.4.4 *The clinical findings.*

The number of patients referred who were found to have no DR during the four years did not vary greatly (484, 473, 466 and 512).

The number of patients referred who were found to have mild to moderate background DR increased during the first round of screening and remained at a higher level (162, 196,194, and 212).

The number of patients referred who were found to have sight-threatening retinopathy (those in categories 2-9 in Table 35) showed a rise during the first two rounds of screening. There was then a slight reduction but not to the level of the year before the screening programme commenced (172, 247, 268, 236).

The number of patients found to have cataract has shown a gradual rise over the four years (233, 247, 256, and 282). The number of patients found to have glaucoma has remained fairly stable (56, 56, 57, and 69). The number of patients found to have macular degeneration has not shown any particular trend although there have been some fluctuations (106, 85, 102, 79).

4.4.5 *The workload and source of the referral for diabetic retinopathy.*

The total number of referrals for an opinion about diabetic retinopathy showed a steady rise over the four years 227, 333, 363, 368.

The source of referral for an opinion about diabetic retinopathy was GP (62, 30, 13, 22), Optician (via GP) (96, 101, 54, 92), Physician (56, 85, 56, 61) and Eye Screening Service (GDESS) (0, 103, 237, 190).

The source of referral where any diabetic retinopathy was found in the eye clinic was

GP (88, 58, 37, 43), Optician (via GP) (124, 119, 73, 108), Physician (64, 90, 65, 57) and Eye Screening Service (GDESS) (0, 104, 233, 184).
The source of referral where sight-threatening diabetic retinopathy was found in the eye clinic was GP (38, 19, 16, 21), Optician (via GP) (60, 49, 30, 34), Physician (35, 49, 28, 24) and Eye Screening Service (GDESS) (0, 71, 155, 115).

4.4.6 *The workload and source of referral of patients with diabetes referred for cataract opinion and reduced vision and the numbers listed for cataract surgery.*

The total number of referrals specifically for cataract opinion was 66,55,74,95. The source of these was GP (19, 14, 13, 19), Optician (via GP) (40, 35, 39, 62), Physician (5, 1, 2, 2) and Eye Screening Service (GDESS) (0, 4, 17, 12). During the four years there was a gradual fall in numbers referred with reduced vision (288, 272, 232, and 221).
The number listed for cataract surgery remained fairly stable (158, 143, 145, and 168).

4.4.7 *The workload and source of referral of patients with diabetes referred specifically for a glaucoma opinion and the numbers of patients with diabetes actually diagnosed with glaucoma.*

The total number of referrals specifically for glaucoma opinion was 56, 61, 59, and 65. The source of these was GP (2, 8, 3, 2), Optician (via GP) (51, 42, 25, 42), Physician (3, 3, 2, 3) and Eye Screening Service (GDESS) (0, 8, 28, 6).
The number of patients with diabetes actually diagnosed with glaucoma was 55, 54, 55, and 62.
The source of referral of those actually diagnosed with glaucoma (even if the referral reason did not suggest this) was GP (11, 12, 8, 12), Optician (via GP) (42, 32, 19, 34), Physician (2, 6, 5, 5) and Eye Screening Service (GDESS) (0, 3, 17, 7).

4.4.8 *False negatives from the retinopathy screening programme.*

The number of false negatives was calculated using the definition:
A patient, who had been screened within the previous 12 months, had not been referred, and who had been found to have sight threatening retinopathy features.
The number of false negatives detected in 1998-9 was 6 and the following 2 years was 14 and 6. Of these 26 patients identified 14 had maculopathy, 2 pre-proliferative DR, 4

proliferative, and 6 advanced. The records of these patients are being re-examined to ascertain the circumstances of these false negatives. However, it should be noted that casualties presenting between their routine clinic appointments with for example a vitreous haemorrhage would be classified as new patients on our Patient Administration System. This might explain the number of advanced cases.

4.4.9 *False positive from the GP, optician and physician referral and from the screening programme.*

This was defined as patients who were referred with retinopathy, found to have no retinopathy, and discharged at first visit.

The false positive numbers using the above definition from GP referrals was 7,6,4,3, from Optician 3, 8,5,10, from physician 4,3,2,3 and from GDESS was 4, 20 and 6.

4.4.10 *Non-attenders from screening presenting with retinopathy.*

During the year 2000-01, 55 non-attendees from the first round of screening presented with sight-threatening diabetic retinopathy.

4.4.11 *Numbers referred for laser treatment (and type of laser treatment) and numbers of laser treatment sessions required over the following year.*

Numbers referred for laser treatment and numbers of subsequent appointments required over the following year is summarised with results from the laser treatment audit in Appendix 11.

Numbers referred for laser treatment for maculopathy over the four years was 61, 94, 81, and 36. The total number of laser treatment sessions required for maculopathy (including those requiring fluorescein first) was 89, 136, 119, and 62.

Numbers referred for laser treatment for preproliferative / proliferative retinopathy over the four years was 16, 30, 30, and 27. The total number of laser treatment sessions required for preproliferative / proliferative retinopathy (including those requiring fluorescein first) was 82, 146, 146, and 137. The total number of laser treatment sessions for sight threatening diabetic retinopathy over the four years was 171, 282, 265, and 199.

Table 36 - Reason given for referral (note – more than one reason can be given in the table).

	1997 – 98	1998 –99	1999 –00	2000-01	
Reason given for referral:	Sub-Total	Sub-Total	Sub-Total	Sub-Total	Total
Reduced Vision	288	272	232	221	1013
Retinopathy Seen	222	328	357	364	1271
Poor view	19	19	28	34	100
History of:					
Non -Specific	15	10	14	11	50
Blurred Vision / Visual Disturbances (Other Than Field Defects)	7	8	13	7	35
Field Defect/ Scotoma	14	9	6	5	34
Pain / Discomfort/ Itchiness/ Grittiness/ Headaches	48	31	36	30	145
Previous Non-Attendance	8	14	18	2	42
Sudden Vision Loss	2	4	3	3	12
Watering	4	6	7	5	22
Post-op cataract	2	2	0	5	9
Opinion about:					
Conjunctival / Scleral/ Red Eye	7	10	6	13	36
Corneal	6	10	5	13	34
Lids	35	14	23	43	115
Diplopia / Nerve Palsy	20	8	22	16	66
Cataract Opinion	64	57	77	93	291
Posterior Capsular Opacification	6	8	14	12	40
Glaucoma Opinion Or Optic Disc Abnormalities Relating To Glaucoma	57	62	61	68	248
Macular Degeneration	3	5	8	9	25
Diabetic Retinopathy	11	16	11	10	48

Iritis / Uveitis/ Endophthalmitis	4	2	0	6	12
Emboli	2	1	2	5	10
Vein Occlusion	2	5	5	6	18
Vitreous Symptoms/Opinion/ Flashes/Floaters	19	23	24	18	84
Vitreoretinal Surgery Opinion	2	2	2	2	8
Non-Specific Opinion Except Retinal/ Miscellaneous	5	11	9	16	41
Non-Specific Retinal Opinion	20	29	29	25	103
Trauma / Burns/ Foreign Body	11	14	6	13	44
Total	903	980	1018	1055	3956
One reason	707	828	824	853	3212
Two reasons	98	76	97	101	372
Missing reasons	48	50	53	97	248
Total attendances	853	954	974	1051	3832

Table 37 - The source of the referral.

	1997 – 98	1998 –99	1999 –00	2000-01	
Source of the referral:	Sub-Total	Sub-Total	Sub-Total	Sub-Total	Total
GP	278	214	166	211	869
GP & Optician	345	339	243	327	1254
Hospital Eye Screening Clinic	1	1	0	0	2
Physician	111	126	90	94	421
Self-Referral	8	16	9	20	53
Eye Screening Service - GDESS	0	146	361	268	777
From within Eye Department e.g. Ophthalmologist, Optometrist or Orthoptist	24	24	23	9	80
A&E Dept	37	32	31	12	112
Other Hospital Consultant (not physician)	2	2	2	0	6
Specialist Diabetic Nurse	1	0	1	0	2
Direct from optician	0	1	1	0	2
Glaucoma screening	0	0	0	1	1
From private practice	1	2	1	1	5
Other Ophthalmology Department outside Glos	1	0	1	0	2
Total	809	903	929	943	3586
Missing information	44	51	45	108	246
Total attendances	853	954	974	1051	3832

Table 38 - The clinical findings – Retinopathy.

	1997 – 98	1998 –99	1999 –00	2000-01	
Retinopathy levels:	Sub-Total	Sub-Total	Sub-Total	Sub-Total	Total
None	484	473	466	512	1935
1) Mild to Moderate BDR	162	196	194	212	764
2) Maculopathy A	84	146	159	130	519
3) Maculopathy B	11	4	17	7	39
4) Maculopathy C	6	6	1	4	17
5) Preproliferative DR	21	29	35	45	130
6) Proliferative DR	12	16	23	21	72
7) Advanced DR	20	21	14	11	66
8) Photocoagulation from previous Rx	17	22	19	18	76
9) Maculopathy responsible for VA of 6/36 or less	1	3	0	0	4
Sub-total – patients with Sight-threatening DR (2-9 in this table)	172	247	268	236	923
Impossible to classify due to poor view	3	9	3	9	24
Total	821	925	931	969	3646
Missing data	32	29	43	82	186
Total attendances	853	954	974	1051	3852

Table 39 - The clinical findings – Other Eye Diseases.

	1997 – 98	1998 –99	1999 –00	2000-01	
Other Eye Diseases:	Sub-Total	Sub-Total	Sub-Total	Sub-Total	Total
Cataract	233	247	256	282	1018
Glaucoma	56	56	57	69	238
Ocular Hypertension	28	22	12	14	76
Age Related Macular Degeneration/Macular Degeneration	106	85	102	79	372
Conjunctival / Scleral	14	14	16	15	59
Corneal	24	18	18	26	86
Lids Disorders / Entropion / Ectropion / Cysts	45	30	38	54	167
Trauma / Burns/ Foreign Body	11	13	6	11	41
Nerve Palsy	18	11	17	15	61
Complications Of Cataract Surgery	1	1	3	3	8
Posterior Capsular Opacification	25	27	26	19	97
Glaucoma Or Optic Disc Abnormalities Relating To Glaucoma	10	9	21	27	67
Iritis / Uveitis/ Endophthalmitis Not Related To Cataract Surgery	7	12	8	6	33
Emboli	1	4	4	5	14
Vein Occlusion	27	32	19	23	101
Vitreous Changes (Not Diabetic)	21	16	15	17	69
Miscellaneous Non-Retinal	17	35	11	19	82
Miscellaneous Retinal	33	53	51	55	192
Neurological	10	2	8	4	24
Amblyopia	6	7	13	6	32
Thyroid Eye Disease	1	2	1	3	7
Endophthalmitis / Retinitis	1	2	1	0	4

Arterial Problems / CRAO / AION	2	6	7	4	19
Asteroid Hyalosis	3	5	7	4	19
Field Defect - Non-Glaucomatous	7	5	13	2	27
Inherited Defects	3	4	1	2	10
Optic Disc Abnormalities Not Relating To Glaucoma	5	2	3	4	14
Advanced Diabetic Eye Disease	3	0	0	3	6
Total	718	720	734	771	2943

Table 40 – Outcome.

	1997 – 98	1998 –99	1999 –00	2000-01	
Outcome:	Sub-Total	Sub-Total	Sub-Total	Sub-Total	Total
Discharged	175	187	188	139	689
Clinic review for:					
diabetic retinopathy	145	217	227	294	883
other eye disease	270	280	275	334	1159
Listed for laser (see Table 48)	79	129	119	65	392
Listed for YAG laser capsulotomy	17	26	27	16	86
Listed for some other form of laser (e.g. argon for tear or YAG iridotomy)	3	4	3	3	13
Referred for vitreoretinal opinion	5	2	2	4	13
Referred for medical opinion	2	0	0	0	2
Referred for opinion from vascular surgeons	2	1	3	3	9
Referred for subspecialty examination usually within eye department:					
a) Refraction	2	1	1	1	5
b) Low vision clinic	3	4	3	1	11
c) Orthoptic opinion	3	1	5	4	13
d) Visual field examination	4	2	6	13	25
e) Fluorescein angiography	16	18	21	33	88
MRI scan	1	0	0	1	2
Listed for cataract surgery	158	143	145	168	614
Listed for vitreoretinal surgery	1	1	3	2	7
Listed for lid surgery	12	8	8	13	41
Listed for other surgery e.g. glaucoma	2	1	8	4	15
Refused surgery	3	4	0	1	8

Other Outpatient procedure (e.g. removal of corneal fb / sutures, syringing nasolacrimal ducts etc.)	5	6	5	0	16
Registered blind – full BD8	6	3	2	6	17
Registered partially sighted – partial BD8	12	8	6	2	28
Admission	0	0	1	1	2
Vitreoretinal opinion	9	9	6	1	25
Miscellaneous	4	4	6	6	20
Referred to other hospital	0	1	1	1	3
Total	939	1060	1071	1116	4186
Missing outcome	23	18	26	62	129
One outcome	721	812	825	861	3219
Two outcomes	109	124	123	128	484
Total attendances	853	954	974	1051	3832

Table 41 - The clinical findings – Patients referred for fluorescein angiography.

	1997 – 98	1998 –99	1999 –00	2000-01	
	Sub-Total	Sub-Total	Sub-Total	Sub-Total	Total
None	5	2	5	7	19
1) Mild to Moderate BDR	1	7	5	3	16
2) Maculopathy A	5	5	9	15	34
3) Maculopathy B	1	0	0	0	1
4) Maculopathy C	2	2	0	3	7
5) Preproliferative DR	0	0	0	1	1
6) Proliferative DR	1	1	2	0	4
7) Advanced DR	0	0	0	2	2
8) Photocoagulation from previous Rx	0	0	0	0	0
9) Maculopathy responsible for VA of 6/36 or less	1	0	0	0	1
No retinopathy information	0	1	0	1	2
Impossible to classify due to poor view	0	0	0	1	1
Total	16	18	21	33	88
Sub-total – patients referred for fluorescein with maculopathy (1-4 & 9 in this table)	10	14	14	21	59
Sub-total – patients referred for fluorescein with pre or proliferative DR (5-7 in this table)	1	1	2	3	7
Patients referred at first visit for laser for maculopathy as well as fluorescein for any DR	3	4	3	1	11
Patients referred at first visit for PRP laser as well as fluorescein for any DR	0	1	2	2	5
Patients referred for fluorescein alone at first visit for maculopathy	7	10	11	20	48
Patients referred for fluorescein alone at first visit for pre or proliferative DR	1	0	0	1	2

Table 42 - False negatives from the retinopathy screening programme.

	1997 – 98	1998 –99	1999 –00	2000-01	
The clinical findings:	Sub-total	Sub-total	Sub-total	Sub-total	Total
A patient who had been screened within the previous 12 months, had not been referred, and who had been found to have the following:	Not applicable (before screening commenced)				
Maculopathy A		2	7	5	14
Maculopathy B		0	0	0	0
Maculopathy C		0	0	0	0
Preproliferative DR		1	1	0	2
Proliferative DR		2	2	0	4
Advanced DR		1	4	1	6
Maculopathy responsible for VA of 6/36 or less		0	0	0	0
Total		6	14	6	26

Table 43 - False positive from the GP, optician and physician referral and from the screening programme.

(Defined as patients who were referred with retinopathy who were found to have no retinopathy and were discharged at first visit).

	1997 – 98	1998 –99	1999 –00	2000-01	
	Sub-total	Sub-total	Sub-total	Sub-total	Total
GP referrals	7	6	4	3	20
Optician referrals (GP + Optician) and occasional optician direct	3	8	5	10	26
Physician referrals	4	3	2	3	12
Eye Screening Service (GDESS)	Not applicable	4	20	6	30
Total	14	21	31	22	88

Table 44 - Non-attenders from screening within the previous 24 months presenting with retinopathy:

	1997 – 98	1998 –99	1999 –00	2000-01
	Not applicable until the second round of screening had commenced.			Total
Maculopathy A				29
Maculopathy B				1
Maculopathy C				1
Preproliferative DR				9
Proliferative DR				8
Advanced DR				7
Maculopathy responsible for VA of 6/36 or less				0
Total				55

Table 45 - The change in workload during the first round of screening (middle 2 years).

Source of referral to Eye Clinic with referral criteria of Diabetic Retinopathy seen or opinion about Diabetic Retinopathy:

	1997 – 98	1998 –99	1999 –00	2000-01	Total
	Sub-total	Sub-total	Sub-total	Sub-total	
GP	62	30	13	22	127
GP & Optician	96	101	54	92	343
Hospital Eye Screening Clinic	0	1	0	0	1
Physician	56	85	56	61	258
Self-Referral	0	0	0	0	0
Eye Screening Service - GDESS	0	103	237	190	530
From within Eye Department	10	11	3	3	27
A&E Dept	1	1	0	0	2
Other Hospital Consultant (not physician)	0	0	0	0	0
Specialist Diabetic Nurse	0	0	0	0	0
Direct from optician	0	0	0	0	0
Glaucoma screening	0	0	0	0	0
From private practice	0	1	0	0	1
Other Ophthalmology Department outside Glos	0	0	0	0	0
Total	225	333	363	368	1289

Table 46 - The change in workload during the first round of screening (middle 2 years).

	1997 – 98	1998 –99	1999 –00	2000-01	
Numbers referred to Eye Clinic with Any Diabetic Retinopathy found in clinic from:	Sub-total	Sub-total	Sub-total	Sub-total	Total
GP	88	58	37	43	226
GP & Optician	124	119	73	108	424
Hospital Eye Screening Clinic	1	1	0	0	2
Physician	64	90	65	57	276
Self-Referral	3	7	3	6	19
Eye Screening Service – GDESS (See table 46)	0	104	233	184	521
From within Eye Department	13	17	11	6	47
A&E Dept	7	7	4	2	20
Other Hospital Consultant (not physician)	0	1	1	1	3
Specialist Diabetic Nurse	0	0	0	0	0
Direct from optician	0	0	1	0	1
Glaucoma screening	0	0	0	0	0
From private practice	0	1	1	0	2
Other Ophthalmology Department outside Glos	1	0	1	0	2
Total	301	405	430	407	1543

Table 47 - The change in workload during the first round of screening (middle 2 years).

Numbers referred to Eye Clinic with Sight-threatening Diabetic Retinopathy found in clinic from:

	1997 – 98	1998 –99	1999 –00	2000-01	
	Sub-total	Sub-total	Sub-total	Sub-total	Total
GP	38	19	16	21	94
GP & Optician	60	49	30	34	173
Hospital Eye Screening Clinic	0	0	0	0	0
Physician	35	49	28	24	136
Self-Referral	3	6	3	5	17
Eye Screening Service - GDESS	0	71	155	115	341
From within Eye Department	11	15	6	4	36
A&E Dept	4	5	2	1	12
Other Hospital Consultant (not physician)	0	0	0	0	0
Specialist Diabetic Nurse	0	0	0	0	0
Direct from optician	0	0	0	0	0
Glaucoma screening	0	0	0	0	0
From private practice	0	1	1	0	2
Other Ophthalmology Department outside Glos	1	0	1	0	2
Total	152	215	242	204	813

Table 48 – Referrals from GDESS (reasons for referral when retinopathy found).

Referred from the GDESS with any Diabetic Retinopathy found in clinic				
	1998 –99	1999 –00	2000-01	
	Sub-total	Sub-total	Sub-total	Total
Reason given for referral:				
Reduced Vision	5	10	5	20
Retinopathy Seen	91	189	156	436
Poor view	2	4	4	10
Other	6	20	5	31
Sub-total	104	223	169	496
Missing information	0	10	15	25
Total	104	233	184	521

Table 49 - Numbers listed for laser treatment (and type of laser treatment).

	1997 – 98	1998 –99	1999 –00	2000-01	
	Sub-total	Sub-total	Sub-total	Sub-total	Total
New patients listed for:					
1) No retinopathy	2	4	6	2	14
2) Mild to mod background DR	1	3	3	1	8
3) Diabetic maculopathy	60	91	78	35	264
4) Preproliferative	5	9	8	5	27
5) Proliferative DR or Advanced DR	8	17	19	20	64
6) Photocoagulation from previous Rx	3	4	3	2	12
Subtotal – patients referred for laser for diabetic retinopathy (categories 2-6)	77	124	111	63	375
7) Unclassified poor view	0	1	1	0	2
Total	79	129	118	65	391

Table 50 - Numbers of diabetic cataract referrals for cataract surgery.

(Source of referral of patients referred to Eye Clinic with Cataract seen or opinion about Cataract).

	1997 – 98	1998 –99	1999 –00	2000-01	
	Sub-total	Sub-total	Sub-total	Sub-total	Total
GP	19	14	13	19	65
GP & Optician	40	35	39	62	176
Hospital Eye Screening Clinic	0	0	0	0	0
Physician	5	1	2	2	10
Self-Referral	0	0	0	0	0
Eye Screening Service – GDESS	0	4	17	12	33
From within Eye Department	2	0	2	0	4
A&E Dept	0	1	0	0	1
Other Hospital Consultant (not physician)	0	0	0	0	0
Specialist Diabetic Nurse	0	0	0	0	0
Direct from optician	0	0	1	0	1
Glaucoma screening	0	0	0	0	0
From private practice	0	0	0	0	0
Ophthalmology dept outside Glos	0	0	0	0	0
Total	66	55	74	95	290

Table 51 - The change in workload during the first round of screening (middle 2 years).

	1997 – 98	1998 –99	1999 –00	2000-01	
Numbers referred to Eye Clinic with Cataract found in clinic from:	Sub-total	Sub-total	Sub-total	Sub-total	Total
GP	76	69	44	56	245
GP & Optician	125	124	113	140	502
Hospital Eye Screening Clinic	0	0	0	0	0
Physician	22	23	18	9	72
Self-Referral	0	2	0	0	2
Eye Screening Service – GDESS	0	17	65	60	142
From within Eye Department	1	2	6	1	10
A&E Dept	1	1	2	1	5
Other Hospital Consultant (not physician)	0	1	0	0	1
Specialist Diabetic Nurse	0	0	0	0	0
Direct from optician	0	0	1	0	1
Glaucoma screening	0	0	0	1	1
From private practice	0	0	0	1	1
Other Ophthalmology Department outside Glos	0	0	0	0	0
Total	225	239	249	269	982

Table 52 - Numbers of Diabetic Glaucoma Referrals and the Source.

Numbers referred to Eye Clinic with probable Glaucoma or opinion about Glaucoma from:	1997 – 98 Sub-total	1998 –99 Sub-total	1999 –00 Sub-total	2000-01 Sub-total	Total
GP	2	8	3	2	15
GP & Optician	51	42	25	52	170
Hospital Eye Screening Clinic	0	0	0	0	0
Physician	3	3	2	3	11
Self-Referral	0	0	0	0	0
Eye Screening Service – GDESS	0	8	28	6	42
From within Eye Department	0	0	1	1	2
A&E Dept	0	0	0	0	0
Other Hospital Consultant (not physician)	0	0	0	0	0
Specialist Diabetic Nurse	0	0	0	0	0
Direct from optician	0	0	0	0	0
Glaucoma screening	0	0	0	1	1
From private practice	0	0	0	0	0
Other Ophthalmology Department outside Glos	0	0	0	0	0
Total	56	61	59	65	241

Table 53 - The change in workload during the first round of screening (middle 2 years).

	1997 – 98	1998 –99	1999 –00	2000-01	
Numbers found in Eye Clinic with Glaucoma diagnosed from:	Sub-total	Sub-total	Sub-total	Sub-total	Total
GP	11	12	8	12	43
GP & Optician	42	32	19	34	127
Hospital Eye Screening Clinic	0	0	0	0	0
Physician	2	6	5	5	18
Self-Referral	0	0	2	2	4
Eye Screening Service – GDESS	0	3	17	7	27
From within Eye Department	0	0	2	1	3
A&E Dept	0	1	2	0	3
Other Hospital Consultant (not physician)	0	0	0	0	0
Specialist Diabetic Nurse	0	0	0	0	0
Direct from optician	0	0	0	0	0
Glaucoma screening	0	0	0	1	1
From private practice	0	0	0	0	0
Other Ophthalmology Department outside Glos	0	0	0	0	0
Total	55	54	55	62	226

4.4.12 *Economic analysis.*

The year on year workload changes was not large in relation to the overall activity of the Ophthalmology Department. There was an increase in total new referrals in people with diabetes of 101 in the first year of the screening programme. Allowing 25 minutes per appointment for new outpatients, this would require the annual equivalent of an additional 4 ophthalmology clinics each staffed by 3 clinicians (each with their own list of patients) with nursing and administrative support. Referral rates stayed at a similar level in the second year of the screening programme and increased again in the third year, which would be the first incidence screen. The initial increase in referrals does appear to be attributable to referrals for diabetic retinopathy but these have remained at a fairly constant level across the three years of the screening programme. It should be noted that referrals from the screening service for diabetic retinopathy fell in 2000-1 but this was matched by increased referrals from other sources. The further increase in total referrals in 2000-1 appears to reflect a more general growth in the workload for patients with diabetes. The direct cost consequences for all new referrals are shown below, followed by the figures for referrals specifically for diabetic retinopathy.

4.4.12.1 *New referrals in people with diabetes.*

Table 54 - New referrals in people with diabetes.

	New referrals	Annual increase (% increase)	Cost per Outpatient Visit (1st visit)	Annual cost increase
1997-8	853			
1998-9	954	101 (11.8)	25.08	2533.28
1999-2000	974	20 (2.1)	25.08	501.64
2000-1	1051	77 (7.9)	25.08	1931.31

4.4.12.2 *New referrals for diabetic retinopathy.*

Table 55 - New referrals for diabetic retinopathy.

	New referrals	Annual increase (% increase)	Cost per Outpatient Visit (1st visit)	Annual cost increase
1997-8	227			
1998-9	333	106 (46.7)	25.08	2658.69
1999-2000	363	30 (9.0)	25.08	752.46
2000-1	368	5 (1.4)	25.08	125.41

Following on from the initial referral visits, some patients were referred on either for diabetic retinopathy or for other reasons, resulting in additional outpatient appointments. These have also been costed as new outpatient visits. Again, diabetic retinopathy accounts for most of the increase in the first year of the screening programme and referrals remain similar in the second year. However, there is a further increase in referrals in the third year, both for diabetic retinopathy and for other eye disease. The direct costs for the outpatient visits are shown below.

4.4.12.3 *Clinic review for diabetic retinopathy.*

Table 56 - Clinic review for diabetic retinopathy.

	Number of patients	Annual increase (% increase)	Cost per Outpatient Visit (1st visit)	Annual cost increase
1997-8	145			
1998-9	217	72 (49.7)	25.08	1806
1999-2000	227	10 (4.6)	25.08	251
2000-1	295	68 (30.0)	25.08	1706

4.4.12.4 *Clinic review for other eye disease.*

Table 57 - Clinic review for other eye disease.

	Number of patients	Annual increase (% increase)	Cost per Outpatient Visit 1st visit	Annual cost increase
1997-8	270			
1998-9	280	10	25.08	251
1999-2000	275	-5	25.08	-125
2000-1	334	59	25.08	1480

The number of patients listed for laser treatment for diabetic retinopathy was identified from the workload study and the resulting number of treatments was estimated on the basis of an audit of laser treatment (Appendix 11). The number of patients requiring treatments for diabetic retinopathy does show the expected pattern of increase when screening is introduced in 1998-9 and falls to below the original level when the screening round (2 years) has been completed in 2000-1. The increase in workload in 1998-9 would be equivalent to 12-15 half day treatment sessions, depending on the number of patients seen on each list. The net reduction in 2000-1 compared to 1997-8 would amount to 3-4 half day sessions. Again, only the direct costs of treatment have been included below. (Note that the annual cost increase has been estimated on the basis of the change in number of treatments before rounding).

4.4.12.5 *Listed for laser treatment for diabetic retinopathy.*

Table 58 - Listed for laser treatment for diabetic retinopathy.

	Number of patients	Annual increase (% increase)	Number of treatments	Annual increase	Cost per treatment	Annual cost increase
1997-8	77		162			
1998-9	124	47 (61.0)	275	113	32.87	3726
1999-2000	111	-13 (-10.5)	257	-18	32.87	-592
2000-1	63	-48 (-43.2)	180	-77	32.87	-2526

Numbers referred for laser treatment and numbers of subsequent appointments required over the following year is summarised with results from the laser treatment audit in Appendix 11.

4.4.12.6 *Listed for YAG laser.*

Table 59 - Listed for YAG laser.

	Number of patients	Annual increase (% increase)	Cost per treatment	Annual cost increase
1997-8	17			
1998-9	26	9 (52.9)	39.87	359
1999-2000	27	1 (3.8)	39.87	40
2000-1	16	-11 (-40.7)	39.87	-439

4.4.12.7 *Fluorescein angiography.*

Unlike the laser treatments, fluorescein angiographies have seen a steady increase over the period with a greater increase in the most recent year. The numbers involved are small, however. Laser treatments required following fluorescein angiography have been estimated from the laser treatment audit.

Table 60 - Fluorescein angiography

	Number of patients	Annual increase (% increase)	Laser treatments not included above	Cost per fluorescein angiography	Annual cost increase including laser treatment
1997-8	16		9		
1998-9	18	2 (12.5)	6	28.04	-42.52
1999-2000	21	3 (16.7)	7	28.04	116.99
2000-1	33	12 (57.1)	17	28.04	665.17

More serious cases of diabetic retinopathy may require vitreoretinal surgery. The numbers (new patients referred at first visit for vitreoretinal surgery) identified in the workload study are very small and although the numbers are higher in years 3 and 4 this could be chance variation. Costs for the referral visit and for surgery are shown below. These patients did not necessarily have inpatient stays associated with their surgery, as the only admissions identified from all the referrals were 1 patient in 1999-2000 and 1 patient in 2000-1. These numbers are so small that additional changes in resource use are unlikely to have occurred.

4.4.12.8 *Referred for vitreoretinal opinion.*

Table 61 - Referred for vitreoretinal opinion.

	Number of patients	Annual increase	Cost per outpatient visit	Annual cost increase
1997-8	5			
1998-9	2	-3	25.08	-75
1999-2000	2	0	25.08	0.00
2000-1	4	2	25.08	50

4.4.12.9 *Vitreoretinal surgery*

Table 62 - Vitreoretinal surgery.

	Number of patients	Annual increase	Cost per operation	Annual cost increase
1997-8	1			
1998-9	1	0	515.47	0
1999-2000	3	2	515.47	1,031
2000-1	2	-1	515.47	-515

Retinal screening will also identify patients with cataract. The number of diabetic patients listed for cataract treatment fell slightly when screening was introduced but subsequently increased to a higher level than before the screening programme was introduced. It seems unlikely that these changes are attributable to the screening programme but illustrate the changing workload due to other factors. The costs for day surgery treatment are shown below.

4.4.12.10 *Listed for cataract.*

Table 63 - Listed for cataract.

	Number of patients	Annual increase (% increase)	Cost per treatment	Annual cost increase
1997-8	158			
1998-9	143	-15 (-9.5)	199.55	-2993
1999-2000	145	2 (1.4)	199.55	399
2000-1	168	23 (15.9)	199.55	4589

All the cost items above are summarised in the table below. The first column includes all of the new referrals and subsequent treatments. No clear pattern of cost change emerges from this. Excluding the cataract treatments, which may have varied for reasons other than the screening programme, produces costs as shown in column 2. This suggests a larger cost increase in the first year of the screening programme, followed by more modest increases, possibly reflecting an underlying upwards trend in workload. In column 3, the costs of initial referrals which were not specifically for diabetic retinopathy have also been excluded and the costs now show only a small increase in the third year of screening. Finally, column 4 includes only diabetic retinopathy related activities and this shows a reduction in cost in the final year but this is quite modest and does not suggest that costs would return to their pre-screening programme levels. In addition to the direct costs shown here, each patient episode would generate secretarial and medical records activity. If this were included, the costs would be slightly higher but the pattern would remain the same.

In order to put these cost changes into context, the changes in total workload have been calculated in terms of clinical sessions. The increases are 39.2 sessions in 1998-9, 0.5 sessions in 1999-2000 and 13.9 sessions in 2000-1.

4.4.12.11 *Summary.*

Table 64 – Summary.

	Total cost change (1)	Total cost change excluding cataract (2)	Total cost change excluding cataract and non DR referrals (3)	DR work only (4)
1997-8				
1998-9	5564.47	8557.38	8682.79	8431.97
1999-2000	1621.70	1222.64	1473.46	1598.87
2000-1	6940.86	2351.73	545.83	-934.00

The overall pattern of the cost results is determined by the workload pattern rather than by the specific costs applied to each activity. To demonstrate this, the Gloucestershire workload results have been costed using the much higher average cost figures from the NSC report. (Cataract surgery was not included and therefore costs including this are unavailable). The results are shown in the table below. There is a much larger cost increase in the first year of screening and there is a large cost saving shown after the two years of screening that formed the first screening round. However, the saving in 2000-1 does not return costs to the pre-screening level; they remain about £20,000 higher. The application of average costs has increased the absolute size of the cost changes but has not affected the underlying pattern. The pattern that is observed appears to be a temporary increase due to the first screening round superimposed on a steadily increase workload.

Table 65 - Gloucestershire workload results costed using NSC figures.

	Total cost change excluding cataract (2)	Total cost change excluding cataract and non DR referrals (3)	DR work only
1997-8			
1998-9	52987.46	53287.46	52687.46
1999-2000	9216.76	9816.76	10116.76
2000-1	-29695.45	-34015.45	-37555.45

These results can now be put into context by considering the assumptions about workload made by the National Screening Committee report. These are summarised in the table below with results from the workload study for comparison.

Table 66 – Comparison between NSC estimates and Gloucestershire situation.

Basis of National Screening Committee calculations	Results from Gloucestershire
The setting.	
Cost estimates were based upon a theoretical health authority with a population of 600,000, of whom 2.5% have been diagnosed as having diabetes.[276]	Gloucestershire has a population of 550,000, of whom 2.53% have been identified as having diabetes.
The costs were based on the assumption that the screening test is conducted as a mobile service, with digital retinal photography with mydriasis, by a screening technician, working in primary care premises.	A mobile screening service was introduced in October 1998 performing digital retinal photography with mydriasis, by a screening technician, in primary care premises.
Cost comparisons were made with health authorities that have ad hoc screening schemes, which were assumed to reach about 60% of patients.	Gloucestershire had an ad hoc scheme prior to the introduction of the screening programme.
Workload assumptions.	
Additional treatments and referrals will occur in the early years of a systematic screening programme.	There was an increase in workload in the first two years of the screening programme (prevalence round).
Where there has been no previous monitoring, 5% of those screened will be treated in the first year, falling to 2% by year 4.	The referral rates with STDR from the screening programme in the three years studied were 1.7%, 3.4% and 2.5% respectively. STDR was still being found in referrals from other sources. In 1998-9, 33% of STDR seen at the Eye Clinic was referred from the screening programme.

	This increased to 64% and 56% in the subsequent 2 years.
The projected costs for a national programme are based on the assumption that 80-90% of diabetic patients attend. However the remaining 10-20% remain at risk, and unfortunately may also be those whose diabetes is not well controlled.	The Gloucestershire programme has had an attendance rate of 74% in the first round, which covers two years. 55 patients (27% of cases) with STDR identified in 2000-1 had not presented for screening in the previous 2 year period.
Opportunistic screening by a wide range of different professionals is likely to lead to a large number of referrals, to either the Ophthalmologist or diabetologist for any retinopathy, and not just for sight-threatening disease.	In the Gloucestershire Primary Care Clinical Audit undertaken in 1996 prior to the introduction of the screening programme: Evidence of retinopathy was found in one in four patients (24%) who were being managed totally in primary care, but who had had their eyes examined by an optician, an Ophthalmologist, or a physician's eye screening clinic. Retinopathy was found in only 9% of patients examined by their GP. Nine out of 10 patients (88%) in whom retinopathy had been found, had then been referred to a consultant Ophthalmologist. However, this continued to be the case across all 4 years in the workload study, with more than 70% of referrals having no retinopathy or mild to moderate. Very few of these cases were false positives, but had been referred for reasons other than retinopathy. This suggests that referrals from GPs and other professionals will continue to contribute to the workload of the Eye Clinic.

The treatment costs included in the National Screening Committee report are estimated on the basis of average costs. Treatment costs in this study identified actual changes in level of resources over the time period covered by the introduction of the screening programme. Some of the key assumptions are listed below. All relevant treatment costs were covered by the study.

Table 67 - Comparison between NSC estimates and Gloucestershire Treatment Costs.

Basis of National Screening Committee calculations	Situation in Gloucestershire
Cost assumptions.	
Laser treatments @ £180 each, 6 patients per session, using frequency double YAG or argon laser (capital cost ~£30,000).	The direct costs of laser treatments were estimated as £32.87 based on one clinician (Associate specialist grade), one nurse and one medical photographer plus costs for drops. The numbers treated in a session ranged between 7 and 9. No additional equipment or facilities were required to accommodate the additional treatment sessions and no capital costs have been included.

Proliferative diabetic retinopathy Cost estimates are based on 2 initial treatments, 2 weeks apart, then a review at 6 weeks, with a possible 3rd treatment, then review 6 monthly for two years, i.e. average of 2.5 treatments and 5 out-patient visits = £750 per case.	The number of treatments was established from the laser treatment audit (Appendix 11). For each patient referred, on average, 1.32 eyes required treatment. The average number of treatments per eye was 3.66. At the costs, the per patient cost would be £159. (If 5 follow up outpatient appointments are included it would add £57 per patient to costs.)
Macular oedema Cost estimates are based on 1 initial laser treatment, then follow up every three-four months for two years, but patients often need more treatment, therefore average of 1.5 treatments plus 8 outpatient visits = £750.	The number of treatments was established from the laser treatment audit (Appendix 11). For each patient referred, on average, 1.32 eyes required treatment. The average number of treatments per eye was 1.05. At the costs, the per patient cost would be £46 (If 8 follow up outpatient appointments are included it would add £90 per patient.)
Symptomatic cases of missed disease. This treatment is likely to involve either much more extensive laser therapy or vitreoretinal surgery. The laser therapy could extend to 4 treatments, each costing £180, plus outpatient follow-up, making a likely cost of £1040 per eye. Vitreoretinal surgery would be complicated by the diabetes, so would involve probably involve 2 inpatient stays each of 2 or 3 days and cost some £3000 per eye, plus £300 for follow-up.	Potential false negatives from the screening programme have been identified and these are being examined to establish if they are true false positives or interval cases. The number of diabetic subjects requiring vitrectomy is very small but new referrals with advanced disease would undergo laser treatment first and more cases may emerge over a longer follow up period. The direct costs of surgery were estimated as £515.47 for each operation. The small number of admissions involved would be unlikely to impact on inpatient costs.

4.5. Discussion.

4.5.1 *Discussion relating to the workload study (study 3).*

The number of people with diabetes referred to the eye department continued to rise over the four years of the study, as did the number of referrals for an opinion about diabetic retinopathy. The workload for laser treatment rose during the first round of screening and was the only workload figure that returned to almost the level in the first year (over the four years 171, 282, 265, 199). The figures have been measured against a background of a rise in the number of diabetic patients in the county rose by 1,400 per annum.

Following a survey in 2000 of screening programmes in the South-West Region, Ulrich Freudenstein and Julia Verne published an editorial[277] in the BMJ. In this editorial, they comment on the differences in referral rates to Ophthalmologists. They found a significant difference in rates of referral from screening programmes depending on criteria for referral of screen detected cataracts. In this study, the Eye Screening service did not have a significant impact on referrals for cataract or glaucoma. For cataract, there is was a small increase in referrals in 99/00 due to GDESS but a similar increase in 00/01 is due to opticians. For glaucoma there is very little in the way of an obvious trend – an increase in referrals from GDESS in 99/00 falls back again the following year and there is an increase in optician figures in 00/01. The overall numbers of referrals for a glaucoma opinion remained fairly level.

5 Summary of the three studies.

The original aims of the study have been achieved with the following results:

1. The validation study reported the best results of an Ophthalmologist's examination in the current literature and validated the use of this Ophthalmologist's examination as a reference standard in the main evaluation study (study 2).
2. Two-field digital photography performed well with sensitivities of >80% and specificities of >92% against both reference standard.
3. A useful method of comparison between the Gloucestershire grading form and the Modified Airlie House Grading Classification[266] used for the 7-field stereophotographs, which can be used in further studies (appendix 5).
4. For single-field non-mydriatic photography the sensitivity was 86.0% (CI, 80.9-91.1%), the specificity was 76.7% (CI, 74.5-78.9%). For two field mydriatic photography, the sensitivity was 87.8% (95% CI, 83.0 - 92.6%) and the specificity was 86.1% (95% CI, 84.2 – 87.8%). The difference in specificity was caused by an increase in technical failure rate in the non-mydriatic group (from 3.7% to 19.7%).
5. No alteration in sensitivity or specificity was demonstrated from the addition of technician direct ophthalmoscopy.
6. The organised screening programme was more expensive than the previous opportunistic arrangements but detected more cases of sight threatening diabetic retinopathy. The additional cost per additional case detected was £886. This cost would be reduced if higher throughput levels than 13.3 per day were achieved (as has already been achieved in Gloucestershire).
7. The number and hence cost of all ophthalmology referrals for diabetic patients increases in every year, both during and after the first round of screening. For laser treatment workload alone, the costs do fall after the first round of screening and almost return to the level of pre-screening. These workload and costs are driven by the pattern of workload increases and are not affected by the unit costs applied to activities. The pattern of workload increases are driven by the rise in numbers of people with diabetes in the county.

6 Conclusion.

The validation study has shown that slit-lamp biomicroscopy by an Ophthalmologist, experienced in retinal examination, can compare favourably with seven-field stereo photography as a reference standard when assessing different methods of screening for diabetic retinopathy. There are advantages and disadvantages with both reference methods. There is no hard copy for the Ophthalmologist's slit lamp biomicroscopy and one cannot necessarily conclude that this examination, with different Ophthalmologists, will produce consistently high quality results. However, this paper has highlighted the high technical failure rate of seven field stereo-photography, which even with the most experienced photographers[211] can be 10%, and the technical failure rate for this procedure has not often been reported in previous literature.

The results of the main evaluation study are the first to emerge from a large community based study of digital imaging photography as a screening method. Two 45 degree field mydriatic digital photography has been clearly shown to be a successful screening method and provides a good evidence base to support the recommended method of screening by the English National Screening Programme for Sight Threatening Diabetic Retinopathy. It also provides some support for the three stage screening procedure recommended in Scotland as was recognised by the HTBS and hence the current study was extensively reviewed in their report[12]. Their analysis of the data from this study does make certain assumptions that have been discussed in the previous section and these assumptions would need to be addressed in future research to further validate their approach. The current study also provides some support for the Northern Irish approach of only dilating those aged over 50 yrs because of the low technical failure rates of non-mydriatic digital photography found less than 50 years of age.

The workload study has shown quite high numbers of referrals from other sources after the introduction of the screening programme. GPs, opticians and other professionals continue to refer significant numbers of diabetic patients despite the introduction of the screening programme. This may have been because of the many eye conditions for which diabetic patients night be referred, but referrals for an opinion about diabetic retinopathy reduced from GP's but not from Optometrists who have always been a

greater source of referral. One of the crucial assumptions made by the 2000 National Screening Committee report[7 8] is that by year 4 it should be possible to fund an organised screening programme from revenue savings. A significant part of this saving was assumed to come from resources currently employed in the ad hoc screening of diabetic patients. This study of case records over a 4-year period does suggest that the specific workload related to diabetic retinopathy continues to rise except for laser treatments where the numbers fell after the first round of screening to almost the prescreening level. This rise may be partly due to increasing numbers of diabetic patients. Hence, it is unlikely that savings would be realised.

Our current Gloucestershire screening programme is only every 2 years and this may have been a factor in the continued numbers of referrals from Optometrists and in the ophthalmology workload. It is hoped that, with an annual programme, a significant number of annual review patients might be discharged to an annual screening photographic review and this might reduce the number of outpatient clinic appointments that are currently required for these patients.

7 Future work.

The current study has produced a very useful database of two-field mydriatic digital images and one field non-mydriatic images on a randomised sample of 1549 patients, that have been validated against a reference standard of an Ophthalmologist's slit lamp biomicroscopy.

This image database will be used for three purposes:

1. To test automated analysis computer systems for detection of sight threatening diabetic retinopathy.
2. A further study on the additional value of the nasal field.
3. To test the Scottish three stage screening procedure further by grading the non-mydriatic single field images first followed by one-field mydriatic single field images on those graded as unassessable from the non-mydriatic images.

A Four Nations Research Group has been formed chaired by Professor Richard Himsworth and further multi-centre work is proposed on:

1. Photographic markers for diagnosis of diabetic maculopathy.
2. Screening for diabetic retinopathy in childhood.

8 Publications.

Publications that are being submitted with the thesis:

1. Scanlon P. (2000) Screening for diabetic retinopathy by digital imaging photography and technician ophthalmoscopy. *Diabetes Technology and Therapeutics*, 2 (2): 283-7
2. Scanlon P. (2001) Digital retinal photography in diabetic eye screening. *Diabetes Technology and Therapeutics,* **3** (2): 187-191
3. Scanlon, P. H., Malhotra, R., Thomas, G., Foy, C., Kirkpatrick, J. N., Lewis-Barned, N., Harney, B. & Aldington, S. J. The effectiveness of screening for diabetic retinopathy by digital imaging photography and technician ophthalmoscopy. *Diabetic Medicine. 2003;* **20** (6), 467-474.
4. Scanlon PH, Malhotra R, Greenwood RH, Aldington SJ, Foy C, Flatman M, et al. Comparison of two reference standards in validating two field mydriatic digital photography as a method of screening for diabetic retinopathy. *Br J Ophthalmol* 2003;**87**(10):1258-63.

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I would like to thank my wife Sally and my children Jennie, Ellie, Alex and Charlotte for their patience during the enormous amount of time that I have spent working on this project.

Large studies like those described in this thesis would not be possible without help from a numerous people. I would like to thank those people whom I have listed below as contributors to the individual projects.

9.1 Researchers engaged in the validation study 1

Name	Title	
Scanlon P	Lead Researcher	Original idea for the screening programme and for the research. Applied for the South-West R&D grant. 110 reference standard examinations in Oxford. 129 reference standard examinations in Norwich.
Malhotra R	Researcher	Helped to co-ordinate aspects of the Oxford/Norwich validation study. For example Dr Scanlon was not allowed to know the percentage of patients with referable retinopathy. Graded the digital images from this study.
Foy C	Statistician	Statistical advice and analysis.
Lipinski H	Senior grader	Retinopathy Grading Centre, Imperial College.

		Primary grading of seven-field stereo photographs.
Aldington S	Director	Retinopathy Grading Centre, Imperial College. Advice & secondary grading of seven-field stereo photographs where there were differences of opinion between the reference standards.
Flatman M	Manager	Norwich Screening Service. 7-field 35 mm photography for the Norwich patients.
Lindsell L	Research Co-ordinator Oxford	Advice and assistance with Oxford Ethics Committee application and with clinic organisation.
Greenwood R	Consultant Physician	Norwich. Patient recruitment and advice.
Downes S	Consultant Ophthalmologist	Oxford. Patient recruitment and advice.

9.2 Researchers engaged in the main evaluation study 2

Name	**Title**	
Scanlon P	Lead Researcher	Original idea for the screening programme and for the research. Applied for the South-West R&D grant. 1549 Reference Standard Examinations in General Practice. 2,062 Non-mydriatic gradings. 450 regrades. . 2,062 Mydriatic gradings.
Malhotra R	Researcher	1549 Mydriatic gradings. 1549 Non-mydriatic gradings. 450 Regrades.

Thomas G	Research Assistant	Data entry of all data onto MDI system. Conducted the health economic survey on 400 patients. Assisted with health Economic data collection.
Ludbrook A	Health Economist	Health Economics Research Unit, University of Aberdeen. Supervision of Health Economic aspects of the study and assistance with analysis of data.
Foy C	Statistician	Statistical advice and analysis.
Other contributors to the main evaluation study 2:		
Sparrow J	Consultant Ophthalmologist	Independent chair of the research project board.
Harney B	Consultant Ophthalmologist	Advice and feed-back on non-reference standard referrals in West Gloucestershire.
Hapeshi J	Manager	Glos R & D Support Unit. Advice.
Aldington S	Director	Retinopathy Grading Centre Imperial College. Advice.
Lewis-Barned N	Consultant Physician	Advice.
Lipinski H	Senior grader	Retinopathy Grading Centre, Imperial College. Grading digital images for inter-observer variability.
Waugh N	formerly Director	of Scottish Health Purchasing Information Centre.
	now	Professor of Public Health at the University of Aberdeen. Advice and input into project design.
Kirkpatrick N	Consultant Ophthalmologist	Advice.

Johnson E	Associate Specialist in Ophthalmology	Advice.
Slattery J	Statistician	Principal epidemiological statistician Health Technology board for Scotland. Advice.
Olson J	Consultant Ophthalmologist	Advice on image quality definitions.
Heggie J	Senior screener	Image and data collection.
Coxell K	Screener	Image and data collection.
Horsfall D	Secretary	Data collection.

9.3 Researchers engaged in the workload study 3

Name	**Title**	
Scanlon P	Lead Researcher	Original idea for the research. Applied for the South-West R&D grant. Data collection from the notes.
Carter S	Research Optometrist	Data collection from the notes. Data entry onto MDI system.
Ludbrook A	Health Economist	Health Economics Research Unit, University of Aberdeen. Supervision of Health Economic aspects of the study and assistance with analysis of data.
Foy C	Statistician	Statistical advice and analysis.
Ratiram D	SHO in Ophthalmology	Data collection from the notes.
Histed M	Research Photographer	Data collection from the notes.
Atan D	SHO in Ophthalmology	Conducted audit of laser treatment, results of which have been shown in appendix 11.
Asteriadis S	SHO in Ophthalmology	Conducted audit of laser treatment, results of which have been shown in appendix 11.

Harney B	Consultant Ophthalmologist	Advice and design of laser treatment audit shown in appendix 11.
Thomas G	Research Assistant	Data input of some data onto MDI system.

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1. Research R & D Project Grant of £119,000 in 1998 (R/21/01.98/Scanlon/R).
2. One year R & D Project Grant of £15,000 in 2001.

9.5 Statement of Consent

These three studies were approved by the Gloucestershire Local Ethics Committee was given prior to the commencement of this study.
The validation study 1 was approved by the Oxford and Norwich Local Ethics Committee prior to the commencement of this study.

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* Addresses of companies mentioned in the above thesis:

- Orion Imaging, The Studio, Oldbury Road, Cwmbran, South Wales NP44 3JU.
- SPSS (UK) Ltd, 1 Floor, St Andrew's House, West Street, Woking, Surrey, GU21 1EB.

11 Appendices

The following appendices are attached:

Appendix	1	Gloucestershire grading form
	2	Gloucestershire screening history sheet
	3	Consent form for the main evaluation study
	4	Protocol for visual acuity measurement
	5	Comparison table for the validation study
	6	Quality of image criteria used
	7	Capital costs for the main evaluation study
	8	Invitation, administration and running costs for the screening service (1998/9 prices)
	9	Survey On Patient Costs
	10	Workload Study Data Collection Form
	11	Laser Treatment Audit for Diabetic Retinopathy

GLOUCESTERSHIRE DIABETIC EYE SCREENING SERVICE

Grader: RS Number: Screening Date: Grading Date:

GRADE	RIGHT EYE	DESCRIPTION	LEFT EYE	GRADE OUTCOME
0	☐	NO DIABETIC RETINOPATHY	☐	0 12/12
1 1a 1b	☐ ☐	MINIMAL NON-PROLIFERATIVE DR ≤5 microaneurysms (> 1 DD from foveal centre) and /or 1 superficial haemorrhage (> 1 DD from foveal centre)	☐ ☐	1 12/12
2 2a	☐	MILD NON-PROLIFERATIVE DR >5 microaneurysms > 1DD from foveal centre and /or ≤ 2 microaneurysms < 1DD from foveal centre and /or ≥ 2 haemorrhages > 1DD from foveal centre and /or Exudates outside the temporal arcades and /or ≤5 Cotton Wool Spots	☐	2 12/12
2b	☐	> 2 microaneurysms < 1DD from foveal centre and /or non grouped exudates within arcades > 1DD foveal centre	☐	
3 3a	☐	MACULOPATHY Haemorrhage < 1DD from foveal centre	☐	Referral 3a 'discretionary'
3b	☐	Exudates < 1DD from foveal centre	☐	3 b,c,d Refer 'soon'
3c	☐	Groups of exudates (including circinate & plaques) within the temporal arcades > 1DD from foveal centre	☐	
3d	☐	Reduced VA not corrected by a pinhole likely to be caused by a diabetic macular problem and/or suspected Clinically Significant Macular Oedema.	☐	
4 4a	☐	MODERATE TO SEVERE NON-PROLIFERATIVE DR Multiple cotton wool spots (>5) and / or multiple haemorrhages	☐	4 Refer 'soon'
4b	☐	and / or intraretinal microvascular abnormalities (IRMA) and / or venous irregularities (beading, reduplication, loops)	☐	
5	☐	PROLIFERATIVE DR New vessels on the disc (NVD) or New vessels elsewhere (NVE) Preretinal haemorrhage and / or Fibrous tissue	☐	5 Refer 'urgent'
6	☐	ADVANCED DR Vitreous haemorrhage, and / or traction / traction detachment and / or rubeosis iridis	☐	6 Refer 'immediate'

GLOUCESTERSHIRE DIABETIC EYE SCREENING SERVICE

TREATED DIABETIC RETINOPATHY

PC

- Photocoagulation scars anywhere
- Focal
- Sectoral
- Panretinal
- Grid

Referral 'discretionary'

- Rescreen 12/12
- Refer:
  - 'urgent'
  - 'soon'
  - 'routine'

OL **OTHER LESIONS** OL

- Cataract
- Cupped disc ? glaucoma
- Drusen
- Retinal Pigment Epithelial (RPE) changes
- Disciform macular scar
- Central or branch RVO
- Unexplained reduced VA
- Naevus
- Arterial Embolus
- Other

Referral 'discretionary'

- Rescreen:
  - 12/12
- Refer:
  - 'urgent'
  - 'soon'
  - 'routine'

Q **QUALITY OF IMAGE** Q

- Fully assessable
- Partially assessable
- Not assessable

? **UNSURE - SUBMIT FOR REVIEW** ?

Have the extra fields altered the probable diagnosis of other lesions that you have given Yes ☐ No ☐

Have the screener's comments from ophthalmoscopy altered the diagnosis of other lesions given. Yes ☐ No ☐

Have the extra fields altered the grade of Diabetic Retinopathy that you have Yes ☐ No ☐

Have the screeners comments from ophthalmoscopy altered the grade of retinopathy given. Yes ☐ No ☐

GLOUCESTERSHIRE DIABETIC EYE SCREENING SERVICE

PATIENT DETAILS **DATE OF SCREENING:**

TITLE: Mr/ Mrs/ Miss/ Ms/ Dr/ Prof/ Rev SEX : Male ☐ Female ☐

SURNAME: _____ DOB: _____

FORENAME: _____ 2nd Initial: _____

ADDRESS _____

_____ Postcode _____

TEL: _____ Hospital number _____

RS number _____ NHS number _____

G.P. DETAILS **Is the patient in the study Yes** ☐ **No** ☐

G.P. NAME: _____ **Gold Standard Examination Yes** ☐ **No** ☐

ADDRESS: _____

TELEPHONE: _____ FAX: _____

DIABETES HISTORY

Year of Diagnosis: _____

Type of Diabetes: Type 1 (IDDM) ☐ Type2 (NIDDM) ☐ Unknown ☐

Current Treatment: Insulin ☐ Tablets ☐ Diet alone ☐ Unknown ☐

Type of Care: G.P. only ☐ Shared ☐ Hospital ☐

Name of Diabetologist: _____ Hospital: _____

Treatment for Hypertension: Yes ☐ No ☐

Other relevant information: _____

I have explained to the patient that the photographs taken will be examined and graded by a specialist at the hospital and reports are sent to the patient's G.P. ☐ ☐

I have also explained that, if any treatment is required, referral will be made after consultation with the family doctor.

OPHTHALMOLOGICAL HISTORY RIGHT LEFT

PREVIOUS LASER TREATMENT(for diab ret): ☐ ☐
CATARACT EXTRACTION: ☐ ☐
IOL IMPLANT ☐ ☐
GLAUCOMA ☐ ☐

OTHER (PLEASE SPECIFY) _____

REGISTERED FULL BD8 ☐ REGISTERED PARTIALLY SIGHTED ☐

Name of Ophthalmologist ----------Hospital attended ----------

Date of next hospital visit _____ Date of last hospital visit _____

Last Optician Visit: Within 1 year ☐ 1 - 2 years ☐ >2 years ☐

Was the IOP measured Yes ☐ No ☐ Don't know ☐ (At optician or hospital)

Was the IOP normal Yes ☐ Being rechecked ☐ Referred ☐

OPHTHALMOLOGICAL FINDINGS AT SCREENING APPOINTMENT

BEST CORRECTED V.A.: RIGHT EYE LEFT EYE

Unaided	With glasses	With pinhole	Unaided	With glasses	With pinhole
☐	☐	☐	☐	☐	☐

LOGMAR:

Rt -0.30 -0.20 -0.1 +0.0 +0.1 +0.2 +0.3 +0.4 +0.5 +0.6 +0.7 +0.8 +0.9 +1.0 +1.1 CF HM PL NPL

Lt -0.30 -0.20 -0.1 +0.0 +0.1 +0.2 +0.3 +0.4 +0.5 +0.6 +0.7 +0.8 +0.9 +1.0 +1.1 CF HM PL NPL

Extra letters **Rt** -0.02 –0.04 –0.06 –0.08 **Lt** -0.02 –0.04 –0.06 –0.08

Total Right .....Unrecordable .....ArtEye Total Left .....Unrecordable .....ArtEye

Tested at 4 metres ☐ 2metres ☐ 1 metre ☐

Logmar Acuity after correction for distance: Right ..... Left .....

WAS A GOOD VIEW OBTAINED **Right** Yes No **Left** Yes No
WITH THE OPHTHALMOSCOPE

IF NO PLEASE INDICATE PROBABLE CAUSE:

G. TROPICAMIDE 1% given RIGHT ☐ LEFT ☐
(Please tick)
DILATION: Good Moderate Poor Good Moderate Poor

EXTRA FIELDS TAKEN: Please specify the fields taken and why: _____

Number of non-mydriatic photos taken .....:
Was the decision to take extra fields influenced primarily Screener's comments on ophthalmoscopy:
by the photograph ☐ or direct ophthalmoscopy ☐ _____

_____

RETINAL PHOTOGRAPHY - PATIENT CONSENT

Surname: Forename: Address: RS No: DOB: GP:	I understand that the images and information that has been obtained from screening/photographing my eyes will form part of my confidential computerised health records. I also agree that the above may be specifically used for the purposes of clinical research into diabetes and improving medical care. Any data used for this purpose will be anonymised.
Signature of patient: Date:	Signature of witness: Date:

PROTOCOL FOR VISUAL ACUITY MEASUREMENT

EQUIPMENT

A RETRO-ILLUMINATED EDTRS LOGMAR CHART (FERRIS-BAILY)
These charts are designed for testing at 4 metres, which is the preferred testing distance. They do have an option for testing at 2 metres if it is impossible to test at 4 metres and at 1 metre for patients with very poor vision. The 4 metre distance should be used whenever possible especially for patients with good vision.

A PLAIN OCCLUDER - To cover the eye not being tested

A PINHOLE OCCLUDER - To differentiate between impaired vision due to uncorrected refraction problems and that due to pathology.

METHOD

1. Always explain to the patient what you are doing. **Don't hurry them.**
2. Sit them at the **correct distance** from the chart - **preferably 4 metres**. The patients are seated in our mobile screening system because this makes it easier for us to match the patient's eye level with the centre of the illuminated light box.
3. If **glasses** or **contact lenses** are worn for distance then **test wearing them**. The aim is to record the patient's best possible corrected vision.
4. The patient is given standard instructions before reading the chart - **do not lean forward, read slowly and guess if unsure**.
5. To measure the visual acuity in the right eye the left eye is covered with the plain occluder and **chart 1** is uncovered in the light box. The patient reads slowly down the chart, letter by letter, beginning with the first letter on the top row. When a letter is read correctly the screener circles this letter on a score sheet with a layout identical to that of the chart. Only one reading of each letter is allowed, so it is important to emphasise careful reading. When the subject has difficulty reading a letter, he or she is encouraged to guess. If the logmar acuity is + 0.1 or greater a **pinhole acuity** is measured. If the pinhole acuity is better than the acuity unaided or the acuity with spectacles, the pinhole acuity is recorded as the **best corrected visual acuity**. If the patient is unable to read the top line at 4 metres the patient is then asked to test whether he or she can read the top line at 2 metres and then 1 metre. After the right eye has been tested, it is covered and the **left eye** is tested in similar fashion using **chart 2**.
6. Since there is a **0.1 LogMAR** unit difference between lines on the EDTRS charts and each line has five letters, **each letter** is assigned **0.02 LogMAR units**. This method of measurement gives a practical method of subtracting 0.02 units for each letter correctly read. It also means that if a letter is missed on a line in which the other letters are correctly read and the patient then starts to read the line below, 0.02 units can be added to the score.
7. For measurement at **2 metres add 0.3 to each score**. For measurement at **1 metre add 0.6 to each score.**
8. For those patients who are unable to read the top line at one metre (ie have a LogMAR acuity of >1.6) they are assigned the following scores:

a) **Ability to see hand movement**	**HM**
b) **Perception of Light**	**PL**
c) **No Perception of Light**	**NPL**
d) **VA unobtainable (uncooperative or unable to do)**	**UO with reason**
e) **Artificial Eye**	**AE**

COMPARISON TABLE IN VALIDATION STUDY

7-F	7-F Description	Cat	2-F / Exam	Description	Cat
10	No retinopathy	A	0	No retinopathy	A
20	Minimal	B	1a	Minimal	B
35a	Mild with loops	F	1b	Minimal with haem	B
35b	Mild with Quest. CWS/VB/IRMA	C	2a	Mild with haem/HE/CWS	C
35c	Mild with haem	C	2b	Mild with Ma/HE	C
35d	Mild with HE=2	C	3a	Maculop with haem<1DD	D
35e	Mild with HE>3 in 1+	C	3b	Maculop with HE<1DD	D
35f	Mild with CWS	C	3c	Maculop with HE groups	D
43a	Moderate with HMA>3 in 4/5	E	3d	Maculop with reduced VA/CSME	D
43b	Moderate with IRMA=2 in 1-3	E	4a	Mod.Severe with CWS/HMA	E
47a	Mod.Severe with both 43	E	4b	Mod.Severe with IRMA/VB	F
47b	Mod.Severe with IRMA=2 in 4-5	F	5	Prolif	G
47c	Mod.Severe with HMA=4 in 2-3	E	6	Advanced	G
47d	Mod Severe with VB = 2 in 1	F	U	unassessable	U
53a	Severe with 2 or more 47s	F			
53b	Severe with HMA>4 in 4-5	E	2c	Treated DR	C
53c	Severe with IRMA>3 in 1+	F			
53d	Severe with VB=2 in 2-3	F			
61a	Mild Prolif with FPE or FPD	G			
61b	Mild Prolif with NVE=2 in 1+	G			
65a	Mod.Prolif with NVE>3 in 1 or NVD=2	G			
65b	Mod.Prolif with VH or PRH=2 in 1	G			
71a	HRC with VH or PRH>3 in 1+	G			
71b	HRC with NVE>3 in 1+ and VH/PRH	G			
71c	HRC with NVD=2 and VH/PRH	G			
71d	HRC with NVD>3	G			
75	HRC with NVD>3 and VH/PRH	G			
81	Advanced DR	G			
88	unasessable	U			
99	unassessable	U			

QUALITY OF IMAGE

This is judged with reference to each eye rather than each image and is judged on the macular view. The nasal view is regarded as a bonus rather than a necessity.

1. Fully Assessable – possible to see the small vessels within the temporal arcades with clarity.

2. Partially Assessable – possible to see the large vessels of the temporal arcades with reasonable clarity

3. Not assessable – the large vessels of the temporal arcades are blurred or $\geq 1/3^{rd}$ of the picture is blurred unless sight threatening retinopathy is detected in the remainder.

Capital costs (1998/99 prices)

Item	Cost	assumed life	annuity factor	EAC
Conversion of room	**6109**	10	7.36009	830
furniture	**1700**	10	7.36009	231
2 VA charts/light boxes	**1800**	10	7.36009	245
2 trolleys for light boxes	**822**	10	7.36009	112
2 cameras	**64625**	5	4.21236	15342
2 trolleys for cameras	**5170**	5	4.21236	1227
computers, 6 work stations	**16176**	3	2.67301	6052
2 jaz drives	**1512**	3	2.67301	566
software	**18000**	3	2.67301	6734
printers	**3595**	3	2.67301	1345
ISDN lines	**1815**	10	7.36009	247
ophthalmoscopes	**810**	10	7.36009	110
mobile phones set up	**100**	3	2.67301	37
Model eyes	**118.3**	10	7.36009	16
training	**1500**	3	2.67301	561
total				33654
annual number of patients				4524
cost per patient				7.4389

Invitation and administration 1998/9 prices

Admin support (secretarial)	**14208**
Telephones	**209**
Mobile phones (rental + calls)	**341**
Printing and stationery	**1549**
Computer consumables	**2049**
Office overheads	
Postage	**709**
Cleaning	**43**
Total	19065
Annual number of patients	6100
Cost per patient invited	3.125409836

Running costs 1998/9 prices

Item	
2 vans (lease)	**7797**
Petrol (travel claims)	**1395**
Warranty on cameras	**2372**
Software support (free for first 2 years)	**2500**
Subtotal	14065
Screener 1	**23364**
Screener 2	**21516**
Ophthalmologist grading (3 sessions)	**12584**
Admin – grading (non-medical)	**10128**
Clinical consumables (mydriatic)	**280**
Sub total	67592
Total	81656
Annual number of patients	4524
	18.05

GLOUCESTERSHIRE DIABETIC EYE SCREENING SERVICE

Dr Peter Scanlon MBBS MRCP
MRCOphth, DCH
Associate Specialist

Jan Heggie RGN ONC (Hons)
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DIABETIC EYE SCREENING SERVICE

SURVEY ON PATIENT COSTS

We are carrying out a survey to find out about the costs incurred by people attending for eye screening and by anyone coming with them. We want to take account of these costs when planning how services are provided.

We would be grateful if you would please spare a few minutes to answer the following questions. Any information that you give is anonymous and strictly confidential.

Thank you for your co-operation. If you have any problems with the questions, please feel free to ask

If you would like a survey form in larger print, please ask Gill Thomas

INFORMATION ABOUT YOU

These questions are to help us to see if there are differences in costs for different types of people using the service. The answers you give will not be used to identify you in any way and will, in any case, be treated in strict confidence.

1. What sex are you? ***(Please tick box)***

Male	1
Female	2

2. What is your age? ***(Please write number in years in space).***

_____

3. What is your employment status? ***(Please tick one box only)***

Full time work	1
Part time work	2
Housewife / husband	3
Retired	4
Unemployed	5
Other	9

4. Where have you travelled from? ***(Please tick one box only)***

Home	1
Work	2

(Please give the name of the town or village you have travelled from in the space below)

_____

TRAVEL COSTS

5. How did you travel to the doctor's surgery today? ***(Please tick all that apply)***

Bus	1
Private car	2
Train	3
Taxi	4
Walk	5
Other	9

If other, please specify: .....

6. How long did it take?

☐ Hours ☐ Mins

7. If you travelled by bus, taxi or train, what was the fare?

£

Return	1
Single	2

8. Will the return journey cost the same? ***(Please tick one box only)***

Yes	1
No	2
Not applicable	9

9. If NO, how much will it cost?

£

10. **If you travelled by private car, how long was the journey (one way)?**

	Miles

11. **How much, if anything, was your parking fee?**

£	

12. **What would you have been doing if you had not come for an eye check?**
(Please tick one box only)

Paid work	1
Housework	2
Child care/caring for dependent	3
Voluntary work	4
Leisure activities	5
Other	9

If other, please specify: .....

13. **How much time will you take off from this activity?**

	Hours		Mins

14. **If in paid work, how much income, if any, will you lose?**

£	

COMPANION'S COSTS

15. **Has anyone come with you today?** ***(Please tick box)***

Yes	1
No	2

If NO, go to question 21

16. **If YES, who accompanied you?** ***(Please tick all that apply)***

Spouse/partner	1
Friend	2
Relative	3
Children	4
Other	9

If other, please specify: .....

17. **If anything, how much has your companion paid in fares (one way)?**

£

18. **What would your companion have been doing if he/she had not accompanied you?** ***(Please tick one box only)***

Paid Work	1
Housework	2
Child care/caring for relative/friend	3
Voluntary work	4
Leisure activities	5
Other	9

If other, please specify: .....

19. **How much time did they take off from this activity?**

Hours Mins

20. **If in paid work, how much income, if any, will your companion lose?**

£

CARE FOR CHILDREN OR DEPENDENTS

21. Did you have to ask someone to look after a child/children/other dependants because you were having an eye check? ***(Please tick box)***

Yes	1
No	2

If NO, go to question 27

22. If YES, what would they have been doing if they had not been looking after a child/dependent for you today? ***(Please tick one box only)***

Paid work	1
Housework	2
Caring for other child / dependent	3
Voluntary work	4
Leisure activities	5
Other	9

If other, please specify: .....

23. How much time did they take off from this activity?

	Hours		Mins

24. If in paid work, how much income, if any, do you think they may have lost?

£

25. Did you have to pay them to look after your child/dependent? ***(Please tick box)***

Yes	1
No	2

26. If YES, how much did you pay?

£

ABOUT YOUR VISIT

27. Did you combine your visit to the surgery with anything else? (e.g. shopping, visiting friends, an appointment with the doctor or nurse) ***(Please tick box)***

Yes	1
No	2

28. If YES, what did you combine the visit with?

_____

29. How long was your appointment? (i.e. from first being seen to leaving the surgery)

	Hours		Mins

30. Was your appointment kept to the right time? ***(Please tick box)***

Yes	1
No	2

31. If NO, for how long was your appointment delayed?

	Hours		Mins

32. Have you incurred any additional costs because of your visit? ***(Please tick box)***

Yes	1
No	2

33. If YES, how much did you spend?

£

ABOUT YOUR LAST EYE CHECK

34. Before this visit, when did you last have drops put in and the back of your eyes checked? ***(Please give your best estimate of the month and year in the space below)***

_____

35. Where was this last eye check?

Doctor's surgery	1
Optician's	2
Hospital	3
Other	9

If other, please specify: .....

COMMENTS

If you have any comments to make about this questionnaire please put them in the space below.

Thank you for taking time to complete this questionnaire.

Now please return this questionnaire to **Gill Thomas**

Appendix 10

Workload Study Data Collection Form

Q1. – Patient details (name, address, DOB, GP and hospital number)

Q2 – Type of care
GP only
Hospital
Shared

Q3 – Date of Referral Letter

Q4 – Date of clinic appointment

Q5 - Route of referral
GP
GP and Optician
Hospital Eye Screening Clinic
Physician
Physician for the elderly
Self-referral
Other - please specify

Q6 – Reason Given for Referral
Reduced vision
Retinopathy seen
Poor view
Other - please specify

Q7 - Date of previous retinal examination
Less than 1 year
Between 1-2 years
More than 2 years
Not known

Q8 - Best corrected Visual Acuity recorded in each eye (Snellen)

Q9 – Date of previous retinal photography (if applicable)
Less than 1 year
Between 1-2 years
More than 2 years
Not known
Not applicable

Q10 - Retinopathy in worst eye (see explanatory notes for definitions)
None
Mild to moderate BDR
Maculopathy A
Maculopathy B
Maculopathy C
Preproliferative DR
Proliferative DR
Advanced DR
Photocoagulation from previous treatment
Maculopathy responsible for VA of 6/36 or less
Impossible to classify due to poor view

Q11 – Other eye diseases
Cataract
Glaucoma
Ocular Hypertension
Age related maculopathy
Other - please specify

Q12 – Action
Discharged
Clinic review for diabetic retinopathy
Clinic review for other eye disease
Listed for laser
Listed for cataract surgery
Referred for vitreoretinal opinion
Fluorescein angiography
Registered partially sighted
Registered blind
Other - please specify

Explanatory notes - definitions of retinopathy used in this study:

- *Mild to moderate background DR* – microaneurysms, haemorrhages, exudates and fewer than 5 cotton wool spots with no other ischaemic features or maculopathy as defined below;
- *Maculopathy A* – Within 1DD of the centre of the fovea: haemorrhages and/or exudates, oedema if detected (within 1DD of the centre of the fovea);
- *Maculopathy B* – Within the major temporal arcades but > 1DD from the centre of the fovea: large circinate or plaque hard exudates within the major temporal arcades
- *Maculopathy C* – Reduced VA not corrected by a pinhole likely to be caused by a diabetic macular problem;
- *Pre-proliferative DR* – Venous irregularities (beading, reduplication, loops) and/or multiple haemorrhages and/or multiple cotton wool spots (>5) and/or intraretinal microvascular abnormalities (IRMA);
- *Proliferative DR* – New vessels on the disc or elsewhere in the retina, preretinal haemorrhage and/or fibrous tissue;
- *Advanced DR* – Vitreous haemorrhage, traction / traction detachment or rubeosis iridis.

Appendix 11

Laser Treatment Audit For Diabetic Retinopathy

Number of patients in audit	=	121	
New patients October 98 – October 2000			
Distribution of patients			
Cheltenham	=	58	(48%)
Gloucester	=	63	(52%)
Number of eyes involved in audit	=	160	
Group B (Proliferative)	=	31	(19.4%)
Group A (Maculopathy)	=	129	(80.6%)

Summary of Treatment for Proliferative Diabetic Retinopathy:

Number of eyes = 31
For the initial course of treatment there were a total number of 83 treatment sessions in 31 eyes. The average number of treatments was 2.68 per eye.
Further treatment was often needed during the follow up period of the audit (1 year) - information was available on 29 eyes.
Total treatment sessions for PRP was 102 and 4 eyes had an extra treatment session for associated maculopathy = total 106 treatments.
The average number of treatments was **3.66 per eye** in the first year after diagnosis.
Grade of Doctor performing PRP for proliferative diabetic retinopathy:
19% of treatments for proliferative diabetic retinopathy were performed by a **Consultant, 39%** by an **Associate Specialist** and **42%** by a **Staff Grade**.

Summary of Treatment for Maculopathy:

Number of eyes = 129
(115 received focal laser and 14 received grid treatment)
For focal and grid laser, there were a total number of 136 treatment sessions in 129 eyes. The average number of treatments was **1.05 per eye**.
Grade of Doctor performing focal or grid treatment for maculopathy:
12.4% were performed by a **Consultant, 44.2%** by an **Associate Specialist** and **43.4%** by a **Staff Grade**.

Patients Receiving Fluorescein Fundus Angiography:

All patients receiving Fluorescein Angiography at GRH in this audit between August 1998 and December 2000 were matched against the 503 patients receiving laser treatment during this same period in the GRH laser book.
4 patients were identified with pre / proliferative / advanced Diabetic Retinopathy and 3 received laser treatment **(75%).**
30 patients were identified with maculopathy (or mild to moderate BDR) and 13 received laser treatment **(43.3%).**

Appendix 11 (continued) - Patients listed for laser with any diabetic retinopathy

	1997 – 98	1998 – 99	1999 – 00	2000-01	Total
Patients listed for Laser Rx (focal or grid) for maculopathy / mild to mod BDR (categories 1-4 in table)	61	94	81	36	272
Number of eyes requiring treatment (total x 1.32)	81	124	107	48	360
Total number of laser treatments in one year required for treating these maculopathy patients (total x 1.05)	85	130	112	50	377
Patients referred for fluorescein alone at first visit for maculopathy	7	10	11	20	48
Anticipated number of these fluorescein patients requiring laser for maculopathy 43.3%	3	4	5	9	21
Number of treatments (x1.32x1.05)	4	6	7	12	29
Total laser treatments for maculopathy	89	136	119	62	406
Number of Consultant laser treatments for maculopathy (12.4% total)	11	17	15	8	51
Number of Associate Specialist laser treatments for maculopathy (44.2% total)	39	60	53	27	179
Number of Staff Grade laser treatments for maculopathy (43.4% total)	39	59	52	27	177
Patients listed for Laser Rx (PRP) for proliferative / severe preproliferative / adv DR (categories 4-6 table)	16	30	30	27	103
Number of eyes requiring treatment (total x 1.32)	21	40	40	36	137
Total number of laser treatments in one year required for treating these pre or proliferative / adv DR patients (total x 3.66)	77	146	146	132	501
Patients referred for fluorescein alone at first visit for pre or proliferative / adv DR	1	0	0	1	2
Anticipated number of these fluorescein patients requiring laser for pre or proliferative / adv DR 75%	1	0	0	1	2
Number of treatments (x1.32x3.66)	5	0	0	5	10
Total laser treatments for pre or proliferative / adv DR	82	146	146	137	511
Number of Consultant laser treatments for pre or proliferative / adv DR patients (19% total)	16	28	28	26	98

	1997 – 98	1998 – 99	1999 – 00	2000-01	Total
Number of Associate Specialist laser treatments for pre or proliferative / adv DR patients (39% total)	32	57	57	53	199
Number of Staff Grade laser treatments for pre or proliferative / adv DR patients (42% total)	34	61	61	58	214
The total number of laser treatment sessions for sight threatening diabetic retinopathy	171	282	265	199	917
Total number of Consultant laser treatments for new patients per annum	27	45	43	34	149
Total number of Associate Specialist laser treatments for new patients per annum	71	117	110	80	378
Total number of Staff Grade laser treatments for new patients per annum	73	120	113	85	391
Total number of Consultant laser clinics for new patients per annum (treatments / 6)	4.5	7.5	7.2	5.7	24.9
Total number of Associate Specialist laser treatments for new patients per annum (treatments / 7)	10.1	16.7	15.7	11.4	53.9
Total number of Staff Grade laser treatments for new patients per annum (treatments / 6)	12.2	20	18.8	14.2	65.2